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# Evaluation of cochlear (nerve) implant surgery

Erik Theunisse

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## Proefschrift

ter verkrijging van de graad van doctor  
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## I | Opening

### 1. General introduction

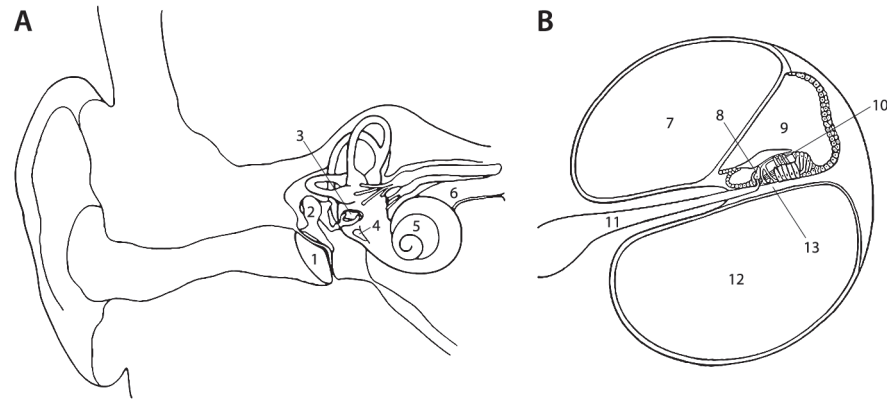


## 1.1. Current state of care in deafness

Nowadays, if a child is born with, or acquires (e.g. as a result of meningitis) severe or profound bilateral hearing loss, in Western Europe standard care consists of bilateral cochlear implantation. Children without additional problems (like cognitive deficits) who receive a cochlear implant at an early age achieve speech perception scores in quiet from 80-95%<sup>1,2</sup>. Approximately 60% of these children can attend mainstream education<sup>3,4</sup>. Attending mainstream education enables them to acquire language and educational levels that are comparable to those of their normal hearing peers<sup>5</sup>. Due to its success, the audiologic criteria for cochlear implantation have shifted over the years from profound to severe bilateral sensorineural hearing loss. In adults, cochlear implantation has become a treatment option for significant age-related hearing loss refractory to hearing aids, and it is even considered for the suppression of unilateral tinnitus<sup>6</sup> and restoring hearing in unilateral sensorineural hearing loss<sup>7</sup>.

## 1.2. The inner ear

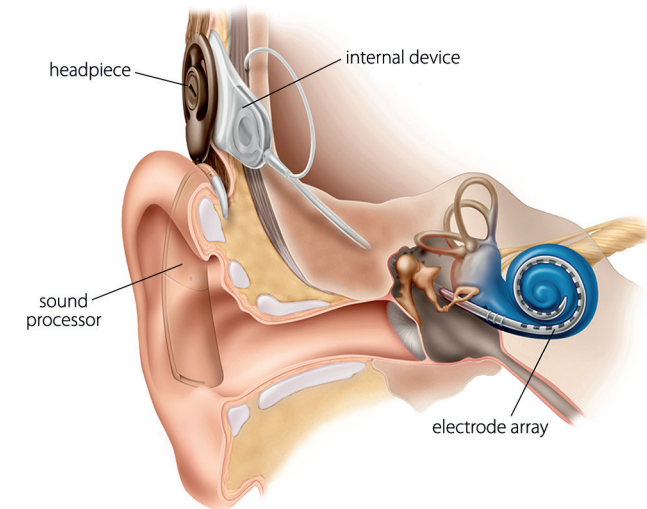
In a normal hearing ear, sound waves are transferred by the tympanic membrane and middle ear ossicles to the peri- and endolymphatic fluid and basilar membrane in the cochlea (Fig. 1). Waves run from the oval window through the scala vestibuli and media to the apex of the cochlea and then back through the scala tympani to the round window. Because of the decreasing stiffness of the basilar membrane (which separates the scala media from the scala tympani) towards the apex of the cochlea, high frequency sounds cause peak amplitudes of the basilar membrane at the base of the cochlea and low frequency sounds cause peak amplitudes more apically. This mechanical property of the basilar membrane forms the basis for cochlear tonotopy. The outer hair cells in the organ of Corti amplify this peak amplitude, resulting in the depolarization of local inner hair cells that release a neurotransmitter which triggers an action potential in the cochlear nerve fibers. This nerve impulse then travels through the brainstem to the auditory cortex where it is perceived as sound<sup>8</sup>. Sensorineural hearing loss is in most cases caused by disorders of the hair cells of the organ of Corti. This inhibits the conversion of pressure waves in the cochlear fluids into nerve impulses.



**Figure 1** **A** Schematic representation of the ear. 1: tympanic membrane; 2: middle ear ossicles; 3: oval window; 4: round window; 5: cochlea; 6: cochlear nerve. **B** Section through turn of the cochlear. 7: scala vestibuli; 8: inner hair cell; 9: scala media; 10: outer hair cells; 11: cochlear nerve fibers; 12: scala tympani; 13: basilar membrane.

### 1.3. Contemporary cochlear implants

The external part of a cochlear implant consists of a sound processor (mostly worn behind the ear) that captures sound with one or more microphones and breaks down its temporal and spectral features through a number of band-pass filters (Fig. 2). The output of each filter corresponds to a different electrode of the implanted array. These signals are conveyed down a cable to the headpiece, which contains a radio frequency transmitting coil and is fixed on the skin by a magnet that is located in the internal device. The transmitting coil sends the coded signals transcutaneously to the antenna of the internal device, which is placed in a bed drilled in the temporal bone. Its electronics package then decodes the radio frequency signals and sends them to the array of electrodes that is inserted in the scala tympani through a fenestration anteroinferior to the round window or through the round window itself. The current from the electrodes directly depolarizes the auditory neurons, bypassing the malfunctioning organ of Corti and the mechanism of neurotransmitter release<sup>9</sup>.



**Figure 2** A contemporary cochlear implant.

### 1.4. Early experiments

Benjamin Wilson is often credited with the first attempt to restore hearing in a deaf person using electricity. In 1748 he used a Leyden jar to administer electric shocks to a 28-year-old woman who was "so deaf as not to hear any one, unless they were very near, and spoke loud to her". After 3 sessions, her hearing improved significantly. Although Wilson suggested that "the cause of this deafness might proceed from some obstruction in the auditory nerves, which might probably be removed by the violent effects of this subtle electric matter", the fact that her deafness "proceeded [...] from a cold" and her hearing improved the most after she blew her nose ("when there issued corrupted matter"), it might be considered that she actually suffered from otitis media with effusion. Especially since experiments on 6 other persons with deafness were unsuccessful<sup>10</sup>.

Alessandro Volta was the first to report the perception of sound induced by electricity in a normal hearing person when he placed two metal rods in his ears that were connected to a battery: "j'ai reçu une secousse dans la tête; et, quelques moments après, (...) j'ai commencé à sentir un son, ou plutôt un bruit, dans les oreilles, que je ne saurois bien définir; c'étoit une espèce de craquement à secousse, ou petillement, comme si quelque pâte ou matière tenace bouillonnait". The experience made him not want to repeat the experiment<sup>11</sup>. Stevens et al., who conducted similar experiments with alternating current on this 'electrophonic phenomenon', reported the identification of different frequencies and even popular



tunes<sup>12</sup>, and were also able to stimulate the auditory nerve in patients without an ear drum and middle ear ossicles by placing an electrode on the oval or round window. They were however, not able to produce auditory sensations in patients who were completely deaf (at least not without stimulating the facial or vestibular nerve), but suggested that *“there may be exceptions to this rule”*<sup>13</sup>. The Swedish neurosurgeon Lundberg was the first to directly stimulate the auditory nerve of a patient during brain surgery in 1950 and *“discovered that the sinusoidal current is perceived not as a tone but as a noise”*<sup>14</sup>.

## 1.5. Development of the cochlear implant

The first electronic auditory implant, was in fact an intraneural implant. In 1957, a by André Djourné developed device was implanted by Charles Eyriès in a patient with bilateral deafness and bilateral facial paralysis after cholesteatoma surgery. During a procedure that was intended for facial nerve grafting, Eyriès inserted an isolated wire electrode in a segment of the cochlear nerve that was exposed through a breach in the labyrinth. Three days later, stimulation with bursts of a 100-Hz impulse signal administered 15 to 20 times per minute led to a sound perception the patient compared with the *“chant de la cigale ou du grillon, ou à des coups de sifflet à roulette”*. And although *“la parole [...] était absolument inintelligible”*, the patient was able to easily recognize simple words in a closed set after a few practice sessions<sup>15</sup>.

Inspired by this research, William House implanted the first true (intrascalar) cochlear implant in two deaf patients in 1961. A single gold wire electrode was placed in the scala tympani (thus not in direct contact with the cochlear nerve) and the patients reported hearing the electrical stimuli. The first patient was reimplanted with a 5-wire electrode array which allowed some basic frequency discrimination and the identification of words in a small closed set<sup>16,17</sup>.

Another intraneural implantation was performed by Simmons in 1964, who implanted a deaf-blind volunteer with a cluster of 6 wire electrodes in the modiolus (the conical shaped central axis of the cochlea where the spiral ganglion of the cochlear nerve is located). The patient reported variations in pitch when different electrodes were stimulated (due to the tonotopy of the cochlear nerve) and also with variations in stimulus frequency (up to 300 pulse/sec)<sup>18</sup>. Nevertheless, cochlear implants were eventually favored over intraneural implants.

In France, a multichannel cochlear implant was developed in which 7 electrodes were introduced in the cochlea through separate fenestrations of the scala tympani. Implantation of 7 patients in 1976 revealed that *“though the intelligibility of word lists remained poor, nearly 50 percent of a usual conversation could be understood without lip reading”*<sup>19</sup>.

The research on intrascalar cochlear implants was boosted when the “Bilger report” (commissioned by The United States National Institutes of Health) was published in 1977.

This was a study on 13 subjects with a functioning (single-channel) cochlear implant that concluded: *“although the subjects could not understand speech through their prostheses, they did score significantly higher on tests of lipreading and recognition of environmental sounds with their prostheses activated than without them”*<sup>20</sup>.

Various multichannel devices that are similar to modern-day cochlear implants were then developed by Ingeborg and Erwin Hochmair in Austria and by Graeme Clark in Australia<sup>21,22</sup>. Tyler et al. traveled to implant centers around the world to test various devices in a uniform way and reported superior speech perception with these multichannel implants<sup>23,24</sup>. A further improvement was achieved when Blake Wilson et al. introduced a new sound processing strategy (Continuous Interleaved Sampling) in 1991, offering speech recognition without lipreading to the majority of the patients<sup>25</sup>.

## 1.6. Limitations

Although cochlear implants have risen far above the initial expectation that they would only be an aid for lipreading, they also have their limitations: they do not restore normal hearing, outcomes vary among patients, performance is considerably degraded by ambient noise, and music perception is limited<sup>26</sup>. Several mechanisms are responsible for these limitations:

- I. The distance between the stimulating electrodes and the target neurons impede efficient stimulation. The site of activation is assumed to be the cell bodies of spiral ganglion neurons or, in some cases, surviving peripheral nerve fibers within the osseous spiral lamina. The electrodes of a cochlear implant are separated from these target neurons or cell bodies by the bony modiolar wall and are bathed in perilymph, an excellent conducting solution. This leads to spread of current in the cochlea, decreased specificity of stimulation and increased electrical current requirements<sup>27</sup>. The resulting overlap of excited neural populations probably limits the number of effective channels to no more than 4-8 (although contemporary implants have 12-22 intracochlear electrodes)<sup>28</sup>, while simulations in normal hearing subjects suggest that speech perception continues to improve up to 10-20 channels, depending on the difficulty of the test<sup>29,30</sup>.
- II. Trauma to the intracochlear structures during insertion of the electrode array (such as fracture of the osseous spiral lamina and disruption of the basilar membrane) may lead to loss of residual hearing or reduced postoperative speech perception scores<sup>31,32</sup>.
- III. It is difficult to access the tonotopic locations representing the lower frequencies, which are located at the apex of the cochlea. This results in a “high-pitch” sound quality upon initial stimulation with standard electrode arrays<sup>33</sup>.

- IV. The envelope extraction algorithms common to cochlear implant signal processing probably lead to a loss of temporal fine structure information<sup>28</sup>.
- V. Cochlear implantation in totally ossified/malformed cochleae often results in poor speech perception stimulation<sup>34,35</sup>. Furthermore, patients with otosclerosis frequently experience facial nerve stimulation<sup>36</sup>.
- VI. The rate of medical complications reported in cochlear implantation is considerable, even up to 63%. Although most of these complications are minor (such as transient taste disorder or vertigo), these also include major complications such as wound infections requiring revision surgery or explantation in 1.6-3.5%<sup>37-39</sup>.

## 1.7. Improving results

There are several ways to overcome the aforementioned limitations. First, by improving implant designs, it may be possible to bring electrode contacts closer to the target neurons (e.g. with modiolar hugging electrode arrays), to reduce trauma to the intra-cochlear structures (e.g. with thinner mid scala electrode arrays) or to achieve deeper insertions (e.g. with long straight electrode arrays). In order to evaluate the clinical effects of such new implant designs, it is important to determine the exact location of the implanted electrodes and the amount of insertion trauma, and correlate this with speech perception scores. Because the latter can only be investigated in clinical trials, this requires reliable (preferably low-dose) high resolution imaging techniques.

There is a need to reduce the number of medical complications in cochlear implantation. Most often, minor complications may be countered and treated effectively. Major complications however have a great impact on CI recipients and frequently lead to loss of the implant. In order to evaluate the magnitude of this important issue, it is necessary to identify the most common and most severe complications. If risk factors can be found for these complications, adjustments in the surgical procedure or perioperative care may lead to a lower complication rate.

A completely different approach is to investigate other sites of electrical stimulation. Because placing electrodes in direct contact with the target neurons reduces stimulation thresholds and spread of excitation, it is worth to reconsider intraneural implantation (see 1.5). Preliminary studies in cats have indeed shown that thresholds for neural excitation are as much as 50-fold lower than with conventional scala tympani stimulation, the interference between electrodes stimulated simultaneously is markedly reduced, and the entire cochlear frequency range (including the lower frequencies) can be accessed<sup>40</sup>. Moreover, this would solve problems with implantation in ossified/malformed cochleae.

## 1.8. Aims and outline of this thesis

Cochlear implantation is a successful treatment for severe to profound bilateral sensorineural hearing loss. This thesis aims to increase this success by addressing three directions for improvement.

The first goal is to find the best low-dose imaging technique for postoperative evaluation of cochlear implantation. This kind of imaging is necessary for the evaluation of new implant designs and research on the relationship between intracochlear electrode positioning and hearing outcome. In part II the possibilities of postoperative imaging using low-dose multi-slice-, and cone-beam computed tomography for evaluating insertion depth, insertion trauma, and precise electrode position are described.

The second goal is to quantify medical complications and device failures in cochlear implantation and to find ways to reduce them, which is the subject of part III. In chapter 3, a method for the uniform registration and classification of complications is proposed. A database system that enables fast and accurate data entry was developed and made freely available. This cochlear implant complication database was applied in chapter 4, which describes the complications and failures of over 1,300 cochlear implantations. These results were analyzed to identify risk factors and to propose means to reduce the number of complications. A novel way to manage postoperative infections using implantable gentamicin-impregnated collagen sponges, is reported in chapter 5.

The third goal is to develop a surgical approach for cochlear nerve implantation, because it may overcome limitations inherent to cochlear implantation. In part IV, the feasibility of penetrating cochlear nerve implantation in humans is explored in a temporal bone and imaging study: in chapter 6 by means of a transcochlear approach that allows access to the modiolus and in chapter 7 by means of a infralabyrinthine approach that allows access to the cochlear nerve and may preserve cochlear integrity.

## II | Postoperative imaging of cochlear implantation

### 2. Cone-beam versus multi-slice computed tomography

**Published as:**

Cone-beam CT versus multi-slice CT systems for postoperative imaging of cochlear implantation--a phantom study on image quality and radiation exposure using human temporal bones.

Theunisse HJ, Joemai RM, Maal TJ, Geleijns J, Mylanus EA, Verbist BM. Otol Neurotol. 2015 Apr;36(4):592-9.



## Abstract

Image quality of low-dose multi-slice computed tomography (MSCT) after cochlear implantation is comparable to that of cone-beam computed tomography (CBCT). CBCT has been described as a low-dose alternative with superior image quality to MSCT for postoperative cochlear implant (CI) imaging, but to our knowledge, no dose-matched comparisons of image quality have been published. Five human cochleae were implanted with CI electrodes and scanned on 2 CBCT and 2 MSCT systems. Four independent observers rated aspects of image quality on a 5-point scale. CBCT scans were compared to clinical and dose-matched MSCT scans. Declining-dose MSCT protocols were compared to the clinical protocol. CT phantoms were used to determine effective dose and resolution for each acquisition protocol. Effective dose of the CBCT protocols was 6 to 16% of the clinical MSCT dose. Visibility of cochlear inner and outer walls and overall image quality were positively correlated with radiation dose on MSCT and image quality was better with clinical MSCT than with CBCT protocols. In other comparisons differences between systems were found, but a distinction between CBCT and MSCT could not be made. CBCT and dose-matched MSCT are both suitable for postoperative CI imaging. Selecting a CT system and radiation dose depends on which cochlear structures need to be visualized.

## 2.1. Introduction

Three imaging techniques are commonly used for postoperative evaluation of cochlear implants: plain X-ray radiography, single-slice or multi-slice (fan-beam) CT and, more recently, flat-panel volume or cone-beam CT (CBCT).

Plain X-ray radiography is a cheap, fast, widely available and low-radiation dose technique, but it does not provide the 3D information needed to assess the configuration of the electrode array.

Multi-slice computed tomography (MSCT) provides information on insertion depth, insertion trauma and precise electrode position<sup>41-46</sup> and allows for visual comparison of different surgical approaches<sup>45,47</sup>. There are, however, differences among MSCT scanners and not all systems allow identification of individual electrodes of a 22-electrode array<sup>48</sup>.

CBCT has been described in multiple studies as a low-dose alternative to MSCT that has superior image quality<sup>49-57</sup>. CBCT systems operate a cone-shaped X-ray beam and provide high-resolution 3D imaging of high contrast structures such as cochlear implants but provide poor soft tissue contrast. In 2002, Husstedt et al. demonstrated the feasibility of imaging intracochlear electrode positions in a temporal bone with a CBCT system incorporated in a biplane digital subtraction angiography system<sup>49</sup>. CBCT was then used to successfully determine the scalar localization of the electrode array in adult patients<sup>58,59</sup>. In 2009, Ruivo et al. also reported that CBCT devices are capable of depicting in vivo cochlear implant arrays with very few artifacts and allow precise assessment of intracochlear electrode position with a fraction of the radiation dose required in MSCT<sup>51</sup>. Direct comparisons of image quality between CBCT and MSCT in the evaluation of cochlear implants in temporal bone specimens were reported, but there were substantial differences in radiation exposure<sup>41,50,52</sup>. To our knowledge, no dose-matched comparisons of image quality have been published.

This study compares image quality of two CBCT and two MSCT systems. The primary objective of this study was to evaluate the radiation dose and image quality of CBCT against clinical and low dose MSCT for postoperative cochlear imaging. The secondary objective was to evaluate the effect of dose reduction in MSCT on image quality.

## 2.2. Materials and methods

### Temporal bones

Five formalin-fixed human temporal bones were implanted with a Nucleus 24 Contour Advance Practice Electrode (Cochlear Ltd, Lane Cove, Australia). This electrode array has a small, non-uniform spacing of the 22 half-banded platinum electrodes (0.8 mm at the basal end to 0.4 mm apically), which makes the highest demands on spatial resolution. After cortical mastoidectomy and posterior tympanotomy, a cochleostomy opening was

drilled anterior and inferior to the round window membrane. The array was inserted using the Advance Off Stylet technique and full insertion was accomplished in all temporal bones. The array was fixed to both the cochleostomy opening and the facial recess using Loctite 495 cyanoacrylate (Henkel, Düsseldorf, Germany) to prevent displacement. The otic capsule and part of the extracochlear electrode array were removed from the temporal bone and used to create human head phantoms. Each phantom consisted of a plastic cylindrical ring with a density similar to bone <sup>60</sup> (0.5 cm thick, 4 cm high and 17.5 cm in diameter) in which the otic capsule (in a latex balloon filled with formalin) was embedded in gelatin in an eccentric position.

Data acquisition

Images were collected using two MSCT systems (Aquilion 64, Toshiba Medical Systems, Otawara, Japan; and Somatom Sensation 64, Siemens Healthcare, Erlangen, Germany) and two CBCT systems (iCAT 3D Imaging System, Imaging Sciences International Inc, Hatfield, USA; and ILUMA Ultra Cone Beam CT scanner, 3M IMTEC Imaging, Ardmore, USA). The phantoms were positioned perpendicular to the axis of the CT scanners to simulate clinical conditions.

To investigate the effect of radiation dose on image quality, MSCT acquisitions were performed at five tube currents (Table 1). The tube current values on MSCT systems were selected to achieve similar radiation dose on both MSCT systems. Other acquisition and reconstruction parameters were adapted from the routine clinical CI protocols. The Sensation 64 did not allow scanning at the lowest effective dose value of 0.03 mSv and, therefore, the lowest dose scan for this system was performed at a tube current of 15 mA. This corresponds with an effective dose of 0.07 mSv. CBCT acquisitions were performed according to manufacturers’ protocols (i.e. one single-acquisition on each CBCT system).

Dosimetry

CT output was evaluated by measuring the normalized computed tomographic dose index assessed with a 100-mm standard pencil dose chamber (CTDI<sub>100</sub>, mGy/mAs) using the clinical CI acquisition protocol in a standard 16 cm cylindrical CT dose head phantom. A calibrated 102-mm-long CT ionization chamber (model CP-4C; Capintec, Ramsey, NJ) was used connected to a dosimeter (model 35050A; Keithley Instruments, Cleveland, Ohio).

Effective dose for MSCT and CBCT acquisitions were estimated by calculating the dose-length product (i.e. multiplying the weighted CTDI [CTDI<sub>w</sub>] with a scan length of 6 cm). To calculate effective dose, this dose-length product was multiplied by a conversion factor of 0.0019 mSv·mGy<sup>-1</sup>·cm (Table 1)<sup>61</sup>. The conversion factor is applicable to CT of the head and effective dose is calculated according to the International Commission on Radiological Protection 103 publication<sup>62</sup>.

**Table 1** Acquisition and reconstruction parameters on two cone-beam computed tomography (CBCT) and two multi-slice computer tomography (MSCT) imaging systems. Associated effective dose values are shown for the acquisitions.

	CBCT		MSCT	
	iCAT	ILUMA	Aquilion 64	Sensation 64
Acquisition parameters				
Tube voltage (kVp)	120	120	120	120
Tube current (mA)	47 (pulsed)	3.8 (continuous)	200-100-50-25-10	139-69-35-17-15*
Rotation time (s)	40	40	0.5	1
Beam collimation (mm)	1 x 60	1 x 60	4 x 0.5	12 x 0.6
Pitch	n.a.	n.a.	0.75	0.45
Reconstruction parameters				
Kernel			FC84	U95u
Radiation dose				
Effective dose (mSv)	0.04	0.10	0.63-0.32-0.16-0.08-0.03	0.63-0.32-0.16-0.08-0.07*

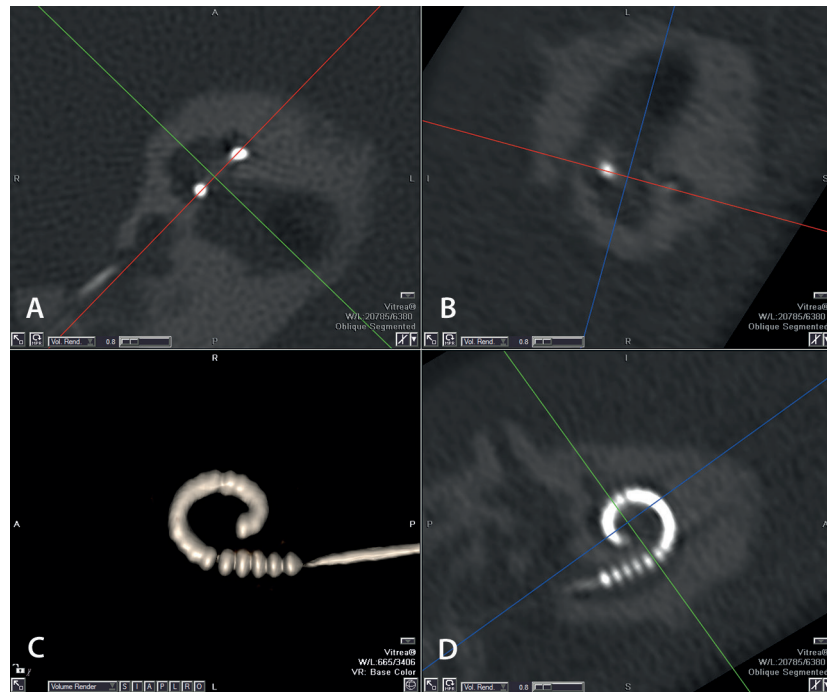
\* The lowest effective dose on the Aquilion 64 was 0.03 mSv (tube current 10 mA), however, the Sensation 64 did not allow scanning at this effective dose value. The lowest effective dose for the Sensation 64 was 0.07 mSv (tube current 15 mA)

Spatial resolution

Measurements of point-spread function (PSF) were performed with a 0.18 mm tungsten bead in a plastic cylindrical phantom of 150 mm diameter. Resolution was quantified by measuring the full-width at half maximum (FWHM) of the PSF curve. Binary images were calculated from the axial images with a threshold at 1000 Hounsfield units (HU). With the binary images, the center of the bead was determined by the recording of pixel values in three dimensions (x, y, and z) as function of distance to the center of the bead over a distance of 5 mm followed by a baseline correction on the resulting curves. FWHM was measured in x and y directions (in-plane) and in z direction (longitudinal).

Subjective image quality assessment

The acquired images were transferred to a dedicated workstation (Vitrea 2; Vital Images, Minnetonka, Minn, USA). Multi-planar reconstructions (MPRs) were created perpendicular to the mid-modiolar axis (plane D, Fig. 1). Four quadrants were defined using a crosshair with its origin on the mid-modiolar axis and the x-axis through the center of the round window. This method is in accordance with the international consensus on cochlear coordinate systems<sup>63</sup>. In addition to the defined MPR plane, two perpendicular planes along the x-axis and y-axis were collected (planes A and B, Fig. 1). These settings were



**Figure 1** Example of multi-planar reconstruction used for the image quality assessment.

One plane perpendicular to the mid-modiolar axis (D) with four quadrants defined using a crosshair with its origin on the mid-modiolar axis and the x-axis through the center of the round window and two additional planes perpendicular along x-axis (A) and y-axis (B). The tip of the electrode is often placed in the same quadrant as the basal portion. Electrode contacts placed beyond the fourth quadrant are referred to as located in the fifth or eventually sixth quadrant.

stored and used by all observers for image quality assessment. Observers were allowed to change the predefined window setting.

MPRs were presented in random order to four observers (blinded to scanner type and dose-level information): a head and neck radiologist with 11 years of experience, a physicist with 5 years of experience, an otologic surgeon with 16 years of experience and an ENT resident surgeon with 3 years of experience in temporal bone imaging. Observers evaluated six aspects of image quality (visualization of electrode position, electrode contacts, osseous spiral lamina and cochlear walls, presence of artifacts and overall impression of scan quality) in A, B or D planes on a 5-point scale ranging from 0 (very poor quality) to 4 (very good quality) (Appendix 1).

### Statistical analysis

Friedman's ANOVA was used to test for differences in image quality ratings between protocols. In case of a significant overall effect, post-hoc comparisons were performed with Wilcoxon signed-rank test (with Bonferroni correction). We completed three analyses for each aspect of image quality:

- Routine clinical CI protocols for all systems (i.e. CBCT protocols versus higher-dose Sensation 64 [309 mAs] and Aquilion 64 [100 mAs] protocols). Wilcoxon test significant at  $p = 0.008$ .
- Routine clinical CI protocols for the CBCT systems and dose-matched protocols for MSCT (i.e. the ILUMA protocol was compared with the 39 mAs Sensation 64 and the 12 mAs Aquilion 64 protocol). Wilcoxon test significant at  $p = 0.017$ .
- Analysis of the effect of decreasing dose for MSCT scans (4 lower dose protocols versus the clinical CI protocol per MSCT system). Wilcoxon test significant at  $p = 0.013$ . Spearman correlation was used to test for correlation between the rated variables and radiation dose.

Inter-observer agreement was evaluated using the mean linear-weighted kappa calculated from the six possible observer-combinations per variable. Kappa values  $< 0.20$  indicate poor agreement;  $0.21 - 0.40$  fair agreement;  $0.41 - 0.60$  moderate agreement;  $0.61 - 0.80$  good agreement; and values  $0.81 - 1.00$  very good agreement<sup>64</sup>

## 2.3. Results

### Temporal bones

CT revealed scala vestibuli position of several contacts in one temporal bone. Full, uncomplicated insertion was achieved in all other temporal bones.

### Dosimetry

The  $CTDI_w$  was measured for the CBCT acquisitions (i.e. 3.7 mGy for the iCAT and 8.6 mGy for the ILUMA). Normalized CTDI was measured for clinical MSCT acquisitions (i.e. 15.4 mGy/100 mAs for the Sensation 64 and 41.99 mGy/100 mAs for the Aquilion 64). Table 2 lists the effective doses.

### Spatial resolution

Spatial resolution of the systems expressed by the full width at half-maximum (FWHM) of the PSF are listed in Table 3. For CBCT systems, longitudinal FWHM was lower than in-plane FWHM whereas MSCT systems showed lower in-plane FWHM (see table). Differences were also found within modalities: the maximum difference within CBCT systems was 43% and within MSCT systems was 29%. The best spatial resolution was found with ILUMA.



**Table 2** Mean parameter ratings and standard deviations in parentheses for the two cone-beam computed tomography (CBCT) and two multi-slice computer tomography (MSCT).

	CBCT				MSCT									
	iCAT	ILUMA	Sensation 64				Aquilion 64							
mAs			309	154	77	39*	33†	100	64	32	50	25	12*	5†
Eff Dose(mSv)	0.04	0.10	0.64	0.32	0.16	0.08	0.07	0.64	0.32	0.16	0.08	0.03	0.08	0.03
ELECT	1.08 (0.87)	3.74 (0.66)	2.84 (1.31)	2.97 (1.33)	2.95 (1.24)	3.06 (1.20)	2.95 (1.19)	0.26 (0.60)	0.22 (0.64)	0.24 (0.57)	0.24 (0.59)	0.28 (0.70)	0.24 (0.59)	0.28 (0.70)
SCALA	2.30 (1.17)	2.40 (1.35)	2.40 (1.00)	2.00 (1.12)	1.95 (1.43)	1.45 (1.05)	1.65 (1.23)	2.70 (1.03)	2.80 (1.15)	3.00 (1.21)	2.90 (1.17)	2.35 (0.99)	2.90 (1.17)	2.35 (0.99)
OSL	0.05 (0.22)	0.15 (0.37)	0.10 (0.31)	0.10 (0.31)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.05 (0.22)	0.00 (0.00)	0.05 (0.22)	0.10 (0.31)	0.15 (0.49)	0.10 (0.31)	0.15 (0.49)
IW	2.40 (1.14)	2.00 (0.92)	2.15 (1.09)	2.40 (1.05)	1.65 (1.23)	1.10 (0.64)	1.10 (0.64)	3.00 (1.08)	2.80 (1.20)	2.70 (1.03)	2.70 (1.22)	1.75 (0.97)	2.70 (1.22)	1.75 (0.97)
OW	2.80 (1.11)	2.55 (0.83)	3.30 (0.87)	3.10 (0.91)	2.85 (0.93)	2.10 (0.79)	1.90 (0.85)	3.70 (0.66)	3.75 (0.64)	3.65 (0.59)	3.45 (0.95)	2.45 (1.00)	3.45 (0.95)	2.45 (1.00)
ARTF	2.10 (1.12)	2.70 (0.47)	2.40 (0.60)	2.70 (0.73)	2.85 (0.67)	2.90 (0.85)	3.25 (0.85)	2.95 (0.61)	3.05 (0.83)	3.20 (0.77)	3.20 (1.01)	3.00 (1.03)	3.20 (1.01)	3.00 (1.03)
OVERALL	1.55 (1.05)	1.70 (0.66)	2.40 (0.88)	2.20 (0.70)	1.75 (0.72)	1.30 (0.66)	1.05 (0.61)	2.05 (0.69)	2.05 (0.61)	1.75 (0.79)	1.95 (0.61)	1.05 (0.51)	1.95 (0.61)	1.05 (0.51)

Mean scores based on 20 evaluations per condition (4 observers x 5 temporal bones) with exception of the visibility of individual electrodes (based on 100 scores, 4 ratings x 5 quadrants x 5 temporal bones). Abbreviations: Eff Dose: effective dose; ELECT: visibility of individual electrode contacts; SCALA: determinability of electrode position (relative to the osseous spiral lamina); OSL: visibility of osseous spiral lamina; IW: visibility of inner wall; OW: visibility of outer wall; ARTF: amount and effect of artefacts; OVERALL: overall scan quality. \* Used for ILUMA dose-matched protocols. † Used for iCAT dose-matched protocols.

**Table 3** Point Spread Function (PSF) measurements per scanner. FWHM: full width at half maximum of the PSF curve.

Variable	FWHM (in mm)			
	iCAT	ILUMA	Aquilion 64	Sensation 64
In-plane	0.75	0.43	0.68	0.48
Longitudinal	0.52	0.39	0.81	0.70
Ratio in-plane/longitudinal	1.44	1.10	0.84	0.69

**Image quality ratings**

Mean ratings over all observers per protocol and mean kappa values are listed in Table 2. Fig. 2 gives an impression of the inter-observer variability by showing the mean ratings of overall image quality of the clinical protocols per observer. Based on the kappa values, the inter-observer agreement for ratings on the visibility of individual electrodes was good; agreement for other variables was fair to poor.

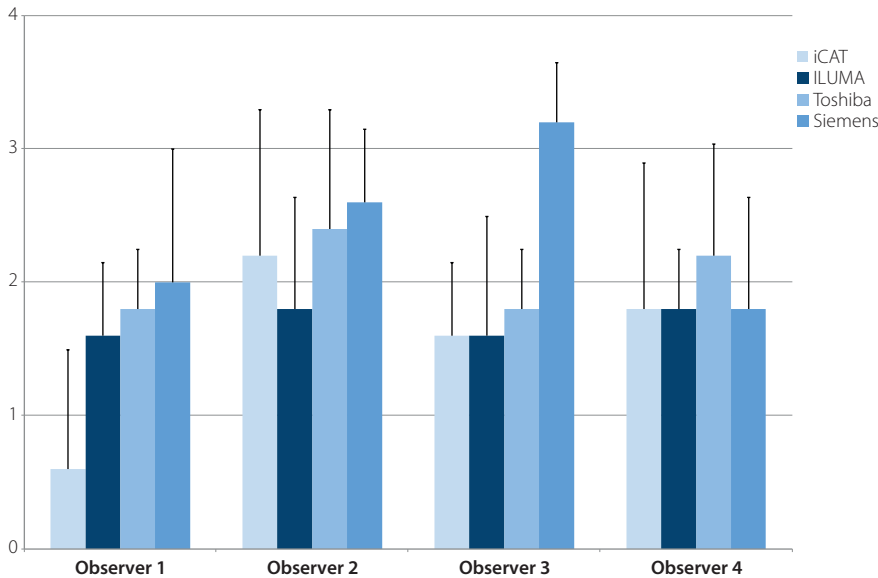
Quadrants of the cochlea were rated separately for the identification of individual electrode contacts to analyze potential differences due to the diminishing spacing between the contacts. For the statistical analysis, we used the mean score pooled over all quadrants because differences between quadrants were similar across systems.

The osseous spiral lamina was not visible or was only vaguely visible in all acquisitions (mean score over all acquisitions and observers was 0.06). No statistical difference was found between any of the protocols for this variable and there was no correlation with protocol radiation dose.

**Clinical CI protocols**

Although there was no main effect of system type (MSCT or CBCT) on *identification of individual electrode contact* ratings, there were significant differences between systems. Results showed that both the ILUMA and Sensation 64 allowed all electrodes to be distinguished from adjacent electrodes (separate at the outer edges and/or fully separate, mean rating  $\geq 2$ ). The remaining two systems were reported as only allowing visualization of some individual electrodes (iCAT) or almost no individual electrodes (Aquilion 64), Fig. 3). Visibility of cochlear walls and overall image quality was rated higher on MSCT than on CBCT systems. Although the *inner and outer cochlear wall* were vaguely or clearly visible over their entire length with all systems (mean rating  $\geq 2$ ), both MSCT systems had a significantly higher rating on outer wall visibility than ILUMA and one MSCT system (Aquilion 64) had a significantly higher rating than iCAT.

*Overall image quality* of the CBCT scans was rated poor to sufficient whereas the MSCT scans were rated sufficient to good. Only a significant difference was found between



**Figure 2** Bar chart of mean ratings per observer of the overall image quality of the clinical CI protocols with standard deviation.

Sensation 64 and iCAT. No clear difference in scalar localization and artifacts was found between MSCT and CBCT systems.

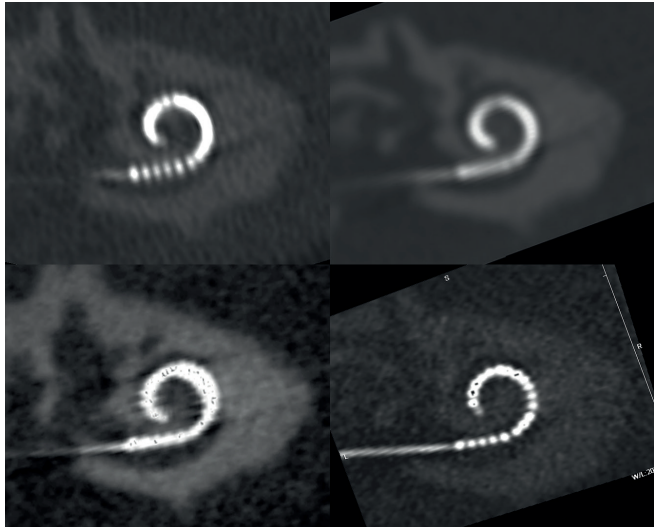
Determination of the *scalar localization* did not significantly differ between any of the systems. For all scans, it was possible to determine the scalar localization of 50-75% of the electrode array (mean rating 2-3). All protocols resulted in mild to medium *artifacts* with a low effect on image evaluation (mean rating 2-3) with Aquilion 64 significantly outperforming iCAT.

a) Dose-matched protocols

*Identification of individual electrodes* had the same pattern of results as the 'Clinical CI protocols'. For all other image quality variables, there was no clear difference between MSCT and CBCT systems (Fig. 4).

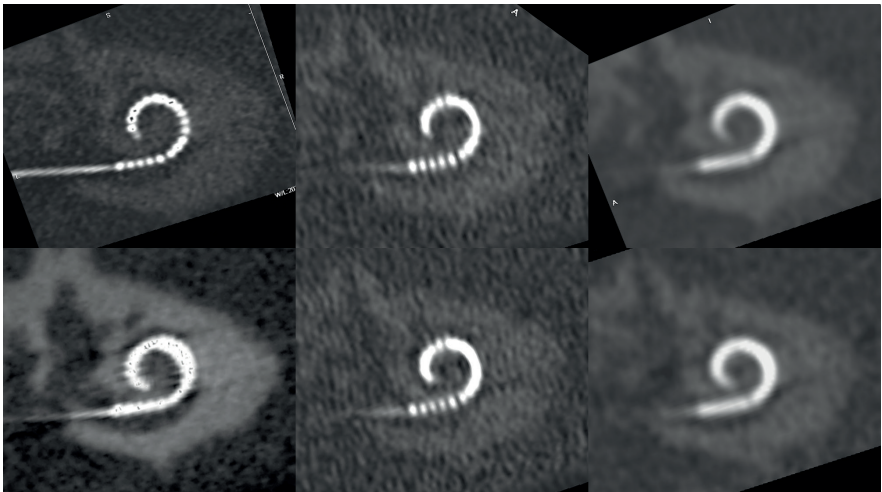
Unlike in the comparison of clinical protocols, the CBCT allowed now similar or better visualization of the *inner wall* than MSCT.

Within the MSCT systems there was a significant between-system difference. The Aquilion 64 was rated as having better visualization of the inner and outer wall and scalar localization than the Sensation 64.



**Figure 3** Images of clinical-dose protocols of the same specimen.

Upper left: Sensation 64 (0.64 mSv), upper right: Aquilion 64 (0.64 mSv), bottom left: iCAT (0.04 mSv), bottom right: ILUMA (0.10 mSv).



**Figure 4** Images of dose-matched protocols of the same specimen.

Upper row (from left to right): ILUMA (0.10 mSv), Sensation 64 (0.08 mSv) and Aquilion 64 (0.08 mSv), bottom row: iCAT (0.04 mSv), Sensation 64 (0.07 mSv) and Aquilion 64 (0.03 mSv).



#### b) Effect of decreasing dose for MSCT protocols

Three image quality variables were negatively affected by reducing the radiation dose: the visibility of the cochlear inner and outer wall and the overall image quality (Friedman ANOVA and Spearman correlation  $p < 0.05$ ). *Inner and outer wall visibility* was significantly reduced in comparison with clinical dose protocols when the tube charge was reduced to 39 mAs with the Sensation 64 and to 5 mAs with the Aquilion 64. The *overall image quality* rating for the Sensation 64 scans was significantly reduced (to below 2 [sufficient]) when the tube charge was reduced to 77 mAs. With the Aquilion 64, ratings of image quality were stable (around 2) until the tube charge was reduced to an ultra low dose level of 5 mAs when image quality significantly decreased. There was no effect of radiation dose on observers' ratings for *identification of individual electrodes*. Reducing radiation dose had a negative effect on *scalar localization* for the Sensation 64 system: 39 mAs resulted in significantly lower ratings compared to 309 mAs. For the Aquilion 64, there was no clear effect of radiation dose and there was no significant overall correlation between radiation dose and *scalar localization* ratings.

For the Sensation 64 system, reducing the radiation dose significantly reduced the amount of *artifacts* (Friedman's ANOVA,  $p < 0.05$ ). The 33 mAs protocol had significantly fewer artifacts than the 309 mAs protocol. For the Aquilion 64 system, no effect of radiation dose on artifacts was found.

## 2.4. Discussion

In this study we compared two CBCT systems with two MSCT systems for evaluating visualization of a 22-electrode contact CI. Our results show that CBCT is adequate for post-operative CI imaging compared to clinical MSCT protocols. There are, however, differences in spatial resolution and perceived image quality between manufacturers' systems<sup>48</sup>. Moreover, CBCTs lack the flexibility of MSCT systems on acquisition and reconstruction parameters (e.g. tube voltage, tube current, reconstruction kernel, slice thickness and slice interval). We have shown that dose reduction on MSCT can be achieved to a dose level similar to CBCT with an image quality comparable to CBCT. In most cases we found that image quality depends on scanner specific features but visualization of the inner and outer cochlear wall and the overall image quality depend on radiation dose.

In the clinical setting CT may be useful for evaluating intracochlear trauma or for frequency mapping in selected cases. Postoperative imaging is also used in research on the relationship between the intracochlear electrode array position and speech perception results and is an essential tool for evaluation of new electrode array designs. The insertion depth (or angle) of the most apical and/or basal electrode is of interest because deep insertion may be associated with trauma<sup>65</sup> and insertion depth may be (negatively)

correlated with speech perception<sup>66</sup>. Scalar localization is important because electrode insertion into the scala vestibuli negatively affects speech perception<sup>66,67</sup> and the traversing of an array from scala tympani to scala vestibuli is an indirect sign of damage to the osseous spiral lamina. The distance between electrode contacts and the inner cochlear wall is thought to be another important factor in speech perception results although evidence is sparse<sup>68,69</sup> and several authors report no clear correlations<sup>70-72</sup>.

To adequately determine insertion depth, it is necessary that scans are not heavily affected by artifacts and that the position of the round window can be assessed (directly or estimated on the basis of the semicircular canal and vestibule<sup>55,73</sup>). Our results show that determining insertion depth is possible with the CBCT and the low-dose MSCT systems used in this study. For the assessment of scalar localization, we found no significant differences between CT systems. As we also found no general effect of radiation dose on scalar localization. Thus, for the MSCT systems, lowering radiation dose to a level that still ensures a sufficient overall image quality may be considered. Although some authors report that the osseous spiral lamina is directly visible on postoperative scans<sup>50,52</sup>, this was not possible with any of the systems in our study.

To directly measure the distance between the electrodes and cochlear walls, both the individual electrode contacts and the inner cochlear wall need to be visualized. The visibility of individual electrodes depends on the intercontact distances. With distances ranging from 0.8 to 0.4 mm between electrode contacts, the CIs used in this study are the smallest currently on the market. The ILUMA reached the required spatial resolution to allow contacts to be distinguished and the Sensation 64 scanner also allowed visualization of individual electrodes. For CIs with larger intercontact distances (e.g. arrays consisting of 12 and 16 contacts) all scanners would have sufficient spatial resolution for visualizing individual contacts. As our results demonstrate, outcomes are system-dependent and are not influenced by radiation dose. Therefore, a system with low radiation dose and spatial resolution that can at least resolve the inter-electrode distance should be used when determining the position of individual electrodes. Visualization of the inner and outer cochlear walls was in most cases better with clinical MSCT protocols than with CBCT protocols. In our study, dose-matched MSCT protocols had comparable ratings of inner and outer wall visibility and overall image quality with CBCT.

Therefore, both CBCT and MSCT can be used for measuring the distance between electrode contacts and the cochlear walls as long as the system has sufficient resolution to allow visualization of individual contacts. For MSCT devices, this should be done with the minimum radiation dose required for adequate visualization of the cochlear walls.

Overall image quality appears related to radiation dose. Clinical MSCT protocols were rated as having better image quality than CBCT protocols (although only significant for the comparison between Sensation 64 and iCAT) whereas the dose-matched MSCT

protocols were rated similar to CBCT protocols. These findings contrast with the only other study comparing a commercially available CBCT system (MiniCAT, Xoran Technologies, Ann Arbor, USA) with a 64-slice CT in which the subjective image quality of the CBCT was rated significantly higher on an ordinal 5-point scale. However, there were no significant differences in measurements of electrode to modiolus distance between CBCT and MSCT and intracochlear array evaluation correlated well with histological evaluation for both techniques<sup>56</sup>. Other performance studies on CI evaluation with CBCT scanners have not compared results with MSCT systems, but report reliable measurements of electrode positions<sup>51,53,55</sup>.

Our study has some limitations. First, we had no access to complete cadaver heads and had to resort to temporal bones. Several studies have used temporal bones for image quality assessment<sup>41,46,47,49,50,52-54,56,57</sup> but this disregards the radiation absorption of a human skull, which may result in larger electrode artifact<sup>43</sup>. To mimic clinical conditions, we created a human skull phantom; preliminary test revealed that there was a considerable difference in image quality between scans of the phantom and of a temporal bone. Second, the inter-observer agreement of the rating of most variables was fair to poor, which may partially be explained by the fact that the observers have different backgrounds. Nevertheless, all have (varying) experience with otologic CT imaging and were trained by the involved radiologist before rating the images. Fig. 2 displays that although there are differences in rating of the clinical protocols between observers, there is considerable agreement on the ranking of the scanners.

## 2.5. Conclusion

Our study shows that both CBCT and MSCT are adequate tools for low-dose postoperative cochlear implant imaging. However, performance differences within CBCT and MSCT systems exist and should be taken into account when choosing an imaging modality, depending on required information for clinical issues or research questions.

## Appendix 1 Ordinal scales used for the image quality assessment.

### Visualization of single electrodes per quadrant

- 0 - No electrodes distinguishable
- 1 - Some electrodes separate from adjacent electrodes at the outer edges
- 2 - All electrodes separate from adjacent electrodes at the outer edges but none fully separate
- 3 - Some electrodes fully separate from adjacent electrodes
- 4 - All electrodes fully separate from adjacent electrodes

### Visualization of electrode position (relative to the osseous spiral lamina)

- 0 - Electrode position cannot be determined
- 1 - ~25% of electrode positions can be determined
- 2 - ~50% of electrode positions can be determined
- 3 - ~75% of electrode positions can be determined
- 4 - All electrode positions can be accurately determined

### Visualization of osseous spiral lamina

- 0 - Not visible
- 1 - Vaguely visible at the modiolar side
- 2 - Clearly visible at the modiolar side
- 3 - Vaguely visible over the entire width
- 4 - Clearly visible over the entire width

### Visualization of cochlear inner/outer wall

- 0 - Not visible
- 1 - Vaguely visible in basal part of the cochlea or at other level than that of the array
- 2 - Vaguely visible over entire length
- 3 - Clearly visible at basal or non-implanted part and vaguely at the rest
- 4 - Clearly visible over entire length

### Presence of artifacts

- 0 - Severe artifacts render image evaluation impossible
- 1 - Severe artifacts heavily affect image evaluation
- 2 - Mild artifacts with some effect on image evaluation
- 3 - Some artifacts without effect on image evaluation
- 4 - No artifacts

### Overall scan quality

- 0 - Very poor
- 1 - Poor
- 2 - Sufficient
- 3 - Good
- 4 - Very good

### III | Complications and failures of cochlear implantation

#### 3. Registration and classification using a custom database

**Published as:**

A database system for the registration of complications and failures in cochlear implant surgery applied to over 1000 implantations performed in Nijmegen, The Netherlands.  
Theunisse HJ, Mulder JJ, Pennings RJ, Kunst HP, Mylanus EA.  
J Laryngol Otol. 2014 Nov;128(11):952-7.



## Abstract

The objective of this study was to create a system for uniform registration and classification of complications and failures in cochlear implantation and apply it to all patients who underwent implantation in our clinic. A definition for a medical complication was established and data from all cochlear implantations between 1987 and 2012 was entered into a custom-made database system. In 19.0% of more than 1,000 cochlear implantations, one or more medical complications were registered; the incidence of hard failure was 2.3%. We found a decrease in device failures over the years and a constant rate of medical complications. Our database system, which is available free of charge, enabled fast and accurate data entry. We found a relatively high number of (minor) complications in our series, but comparison with literature is difficult. This stresses the need for a uniform definition and classification system for complications in cochlear implant surgery.

## 3.1. Introduction

There is a growing demand for quality assessment in medicine. Outcome indicators that can be used are: patient satisfaction, quality of life, mortality and complications. Therefore, uniform registration and classification of complications is essential in order to compare results between medical centers. The shared responsibility for the registration of complications lies with the medical centers and the medical personnel. The key to successful complication registration is to create the infrastructure that warrants an easy, fast and safe means of recording.

Moreover, strict registration of negative outcomes is necessary for the evaluation of new surgical procedures and new devices and also for determining the best policy regarding other management options, such as the necessity of postoperative antibiotic therapy.

Fortunately, severe complications in cochlear implant patients are rare. Therefore, a large number of patients is needed to detect statistical significant differences in complication rates between groups, which can be accomplished by pooling data from different clinics if all the involved centers would be able to use the same system for registration of negative outcomes.

A distinction must be made between complications, sequelae and failures. Complications are unexpected events not intrinsic to the procedure, whereas sequelae are inherent to the procedure, both adding new problems to the underlying disease. Failures are events in which the purpose of the procedure is not fulfilled<sup>74</sup>. In case of cochlear implantation, the procedure itself may be a failure (i.e. a correctly functioning device is implanted without benefit for the patient) or the device itself may be malfunctioning. These device failures are further divided in 'hard failure' (a device with characteristics outside the manufacturer's specification resulting in a loss of clinical benefit) and 'soft failure' (a device malfunction is suspected but cannot be proven using currently available in-vivo methods). Furthermore, a device may have measured characteristics outside the manufacturer's specification, but still be of benefit to the patient<sup>75,76</sup>.

It is also important that a similar definition of a complication is used. In literature, several definitions are used. Clavien and Dindo define a surgical complication as *"any deviation from the normal postoperative course"* (including asymptomatic complications)<sup>74,77</sup>. Rombout et al. define complications in otologic surgery as *"incidents that are not intrinsic to the surgical procedure and that have a potential or actual negative effect on surgical outcome or postoperative morbidity"*<sup>78</sup>. These are very broad definitions that leave room for discussion on what is a complication and what is not.

We adopted the stricter definition of a complication that is given by the Dutch Order of Medical Specialists: *"an unintended and unwanted event or condition during or following medical specialist treatment that is so detrimental for the health of the patient that adjustment of the medical treatment is necessary or that causes irreversible damage"*<sup>79</sup>. This event has to take place during a period from the start of treatment that has been set by the Dutch ENT

association at 6 weeks, but in order to include all possible cases of meningitis and device breakdown may occur at a later instant, we use the criterion that the event *“is (probably) the result of, or has adverse consequences for the implantation”*.

There are also several classification systems that have been used to report complications. For cochlear implantation, Cohen and Hoffman made the distinction between major and minor complications: major complications require additional surgery and/or hospitalization for treatment, while minor complications are treated expectantly and/or with medication alone<sup>80</sup>. A more widely used system in general surgery is the Clavien classification (adapted by Rombout et al. for otologic surgery<sup>78</sup>), which has later been modified into the Clavien-Dindo classification<sup>74,77</sup>. This system uses 5 grades based on patient morbidity:

- Grade I: requiring no/simple measurements (including anti-emetics, antipyretics, analgesics, diuretics, electrolytes and [bedside] seroma drainage)
  - Grade II: requiring pharmacological therapy (including blood transfusions and total parenteral nutrition)
  - Grade III: requiring surgical or radiological intervention
  - Grade IV: requiring IC/ICU management (life-threatening)
  - Grade V: death
- The suffix “d” (for “disability”) is added when the patient suffers from a complication at the time of discharge.

In this paper we present the complications and failures of more than 1000 cochlear implantations, which were registered in a custom database that enables fast and accurate data entry, and grading of medical complications by different classification systems.

3.2. Materials and methods

For data-entry, we created a Microsoft Office Access 2007 (Redmond, WA, United States) database (fig. 1). This is a relational database, which means that any number of implantations could be linked to a patient and any number of complications could be linked to an implantation (fig. 2).

In order to make the system user-friendly and to allow fast and uniform data entry, we created forms with input masks (e.g. for dates) and lookups (a list of preset choices).

For instance, a list of the most common complications in cochlear implantations reported in literature, hard failure and symptoms of soft failure<sup>75</sup> was composed (table 1). To further prevent bad data entry, we implemented required fields and several validation rules (e.g. date of a complication could not be before the date of implantation).

To enable easy classification of the medical complications, we described the consequences of a complication in such a way that both the difference between ‘major’

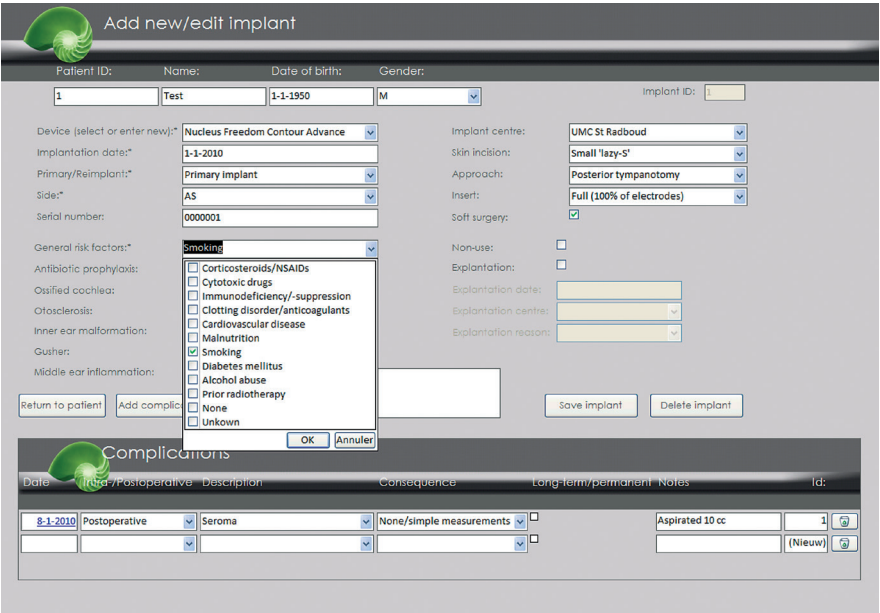


Figure 1 Screenshot from data entry into the database.

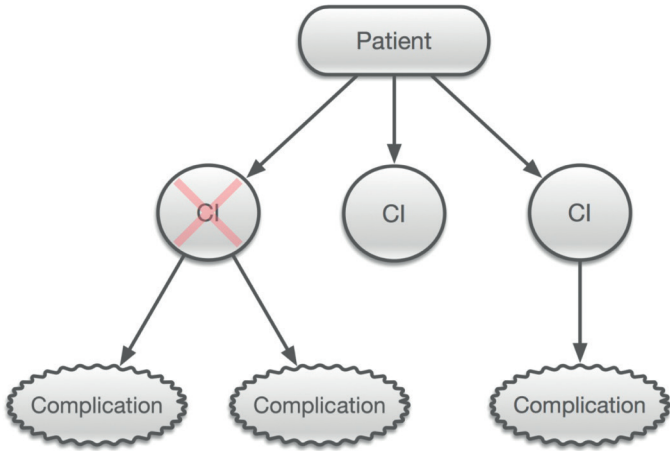


Figure 2 A relational database system.

and ‘minor’ complications could be made and the Clavien-Dindo grading system could be applied. Also, general patient data, such as the etiology of deafness, pneumococcal vaccination and several general risk factors for surgical complications (e.g. diabetes) could be registered.

We built-in an export function that creates an anonymized copy of the database that can be used for analysis by other personnel than the cochlear implant team. By using one-way encryption with a secure hash algorithm (SHA-1), each patient is given a code based on name, birthdate and gender that makes identification of the patient impossible but allows for identification of double entries. This function, in combination with the uniform data entry, also enables the pooling and comparison of data from multiple implant centers.

Data from all cochlear implantations between 1987 and 2012 was entered into the database. The majority of the data was entered retrospectively based on the patients’ charts and from the start of the project, data from new implantations was entered prospectively by members of our cochlear implant team.

3.3. Results

Patient characteristics

The first cochlear implantation in Nijmegen took place in 1987. Between 1987 and 2012, 912 patients underwent a total of 1003 implantations, 470 women and 442 men. Mean age at implantation was 32.5 years (range 0.6-87.6 years), mean follow-up time was 8.6 years (range 1.9-26.8 years). Onset of deafness (best ear) was congenital in 275 cases (30.2%), pre-lingual (< 3rd year) in 165 cases (18.1%) and post-lingual in 392 cases (43.0%). In 53 cases (5.8%) onset of deafness was at an early age, but it could not be determined whether this was pre- or post-lingual and 27 cases (3.0%) were not deaf at time of implantation (Fletcher Index < 90 dBHL). The latter group were patients with severe hearing loss who were implanted based on their speech perception scores (2 patients received an electro-acoustic system); the majority (22 cases) was also deaf at the other ear.

Medical complications

In 191 implantations (19.0%), one or more complications were registered, 208 in total: in 176 implantations (17.5%) one complication occurred during or after implantation, and in 16 cases (1.6%) 2 complications occurred. Of these, 35 were intraoperative and 173 were postoperative. Forty-eight (23%) were classified as ‘major’ and 160 (77%) as ‘minor’ complications. The list of complications graded by the Clavien-Dindo classification is displayed in table 2.

There were 3 cases with postoperative meningitis (0.3%): the first patient was admitted with pneumococcal meningitis, herpes simplex infection, pseudomonas septicemia and

Table 1 The list of complications included in the database.

Description	Type	Intra/Postoperative
Device breakdown	Hard failure	Postoperative
Declining/intermittent performance	Soft failure	
Aversive auditory symptoms		
Facial nerve stimulation		
Other aversive non-auditory symptoms		
Seroma	Medical	
Hematoma		
Wound infection		
Skin flap problems		
Traumatic/pressure skin lesion		
Acute otitis media		
Mastoiditis		
Meningitis		
CSF leak		
Vertigo		
Chorda tympani dysfunction		
Facial nerve dysfunction		
Magnet displacement		
Electrode array dislocation		
Electrode extrusion		
Allergy/rejection		
Pain		
Tinnitus		
Cholesteatoma		
Misplaced electrode array		Intraoperative
Chorda tympani lesion		
Facial nerve lesion		
CSF leak		
Other		Intra-/Postoperative

deep vein thrombosis of the leg; there were no peculiarities during surgery. The second patient had pseudomonas meningitis; during surgery, inner ear malformation (Mondini dysplasia) resulted in perilymphatic gusher. The third patient had pneumococcal meningitis; during surgery, extensive CSF leakage had been found at several locations in the middle ear, necessitating obliteration of the ear (her hearing loss had also been the result of 2 previous episodes of meningitis). The latter two patients had had pneumococcal vaccination before the occurrence of meningitis, the first had not.

**Table 2** Medical complications that were registered in 1003 implantation, graded by the Clavien-Dindo classification.

Complication	Clavien-Dindo grade				Frequency	Percent	Incidence
	I	II	III	IV			
Chorda tympani lesion/dysfunction	40 (3)				40 (3)	19.2	4.0
Seroma	25 (0)	9 (0)			34 (0)	16.3	3.4
Wound infection		26 (0)	5 (0)		31 (0)	14.9	3.1
Pain	4 (2)	9 (2)			13 (4)	6.3	1.3
Traumatic/pressure skin lesion	3 (0)	8 (0)	1 (0)		12 (0)	5.8	1.2
Hematoma	7 (0)	2 (0)	1 (0)		10 (0)	4.8	1.0
Vertigo	4 (0)	5 (1)			9 (1)	4.3	0.9
Mastoiditis		3 (0)	3 (0)		6 (0)	2.9	0.6
CSF leak		2 (0)	1 (0)		3 (0)	1.4	0.3
Electrode extrusion			3 (0)		3 (0)	1.4	0.3
Meningitis		3 (0)			3 (0)	1.4	0.3
Tinnitus	3 (2)				3 (2)	1.4	0.3
Electrode array dislocation			2 (0)		2 (0)	1.0	0.2
Magnet displacement			2 (0)		2 (0)	1.0	0.2
Misplaced electrode array			2 (0)		2 (0)	1.0	0.2
Skin flap problems			2 (0)		2 (0)	1.0	0.2
Facial nerve dysfunction		1 (0)			1 (0)	0.5	0.1
Other	7 (0)	22 (2)	2 (0)	1 (0)	32 (2)	15.4	3.4
<b>Total</b>	<b>93 (7)</b>	<b>90 (5)</b>	<b>24 (0)</b>	<b>1 (0)</b>	<b>208 (12)</b>	<b>100.0</b>	<b>NA</b>

Incidence: percentage of total number of complications; cases with suffix "d" between brackets.

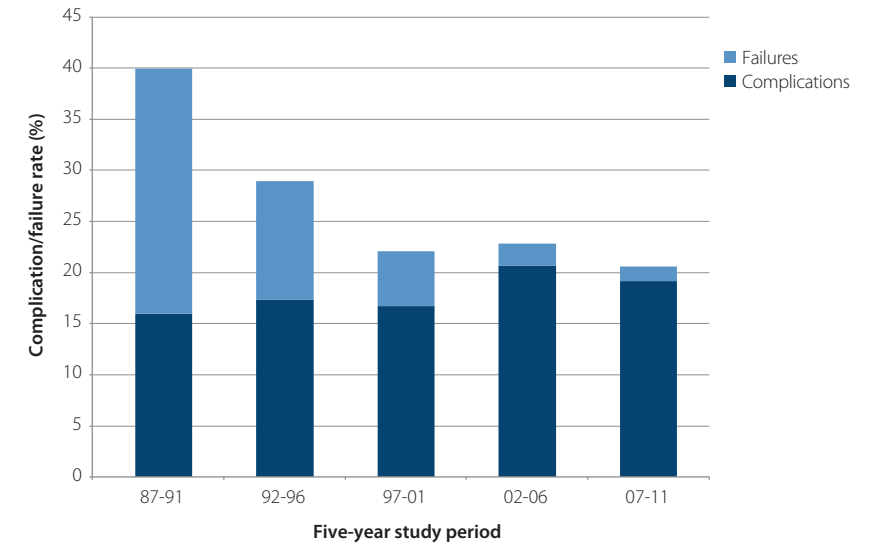
There was 1 case of facial nerve dysfunction (House-Brackmann grade 3), which occurred 2 weeks after implantation on the implanted side and therefore might be unrelated (Bell's palsy). Patient was treated with famciclovir and oral steroids and recovered fully.

There were 8 cases of CI explantation due to a medical complication: 3 cases of a severe wound infection, 2 cases of a misplaced electrode array (1 in hypotympanum and 1 tip-foldover), 1 case of electrode extrusion, 1 case of electrode dislocation and 1 case of CSF leak with subsequent wound infection after closure of the leak had been attempted.

### Device failures

There were 23 cases of hard failure (2.3%), in 2 cases this was after a trauma. All devices were explanted. Of the patients with soft failure, there were 7 with severe facial nerve stimulation; 1 patient had re-implantation and 1 patient underwent cochlear implantation in the other ear. One patient became a non-user and in other cases a substantial number of electrodes could not be used. Other cases of soft failure included two patients with pain when the CI was switched on and 3 cases of declining performance, in 2 of which the CI was explanted and in the other case a CI was implanted in the other ear.

When complication and device failure rate were calculated per 5 years, we found a significant decrease in device failures over the years ( $X^2(4) = 53.64$ ,  $p < .001$ ), while the incidence of medical complications remained fairly constant (no significant difference between 5-year periods) (Fig. 3).

**Figure 3** Complication and failure rates per 5 years of cochlear implantation.



### 3.4. Discussion

Complication registration is important for both quality assessment and research purposes and a uniform definition and classification is essential for comparison of complication data. The custom database we created for this purpose enables fast and accurate data entry and the use of the most frequently used classification systems for surgical complications.

In our series, medical complications occurred in 19.0% of implantations. Incidence of complications reported in literature ranges from 6 to 63%<sup>37-39,81,82</sup>.

There are possible explanations for the relatively high number of complications in our series:

The first reason is that the bulk of our data was obtained by extensive reviewing of medical charts. More than three-quarters of our complications was considered as 'minor' (such as seromas or hematomas) and it is plausible that a number of these would not have been registered as complications in clinical practice.

The second reason is the definition we used, which states that every event that leads to adjustment of the medical treatment is considered a complication. Thus, if any non-routine medication were prescribed (for instance antibiotics for minor redness of the wound), this would be registered as a complication (in this case a wound infection). In our experience, there is a low threshold for prescribing antibiotics in cochlear implant patients for most physicians because of the fear of infection around the implant or even meningitis (in many other countries, postoperative antibiotics are given routinely). This may (partially) explain the high number of wound infection in our series, especially given the fact that the majority was resolved with pharmacological treatment alone (grade II). In many of the aforementioned studies, no definition of a complication was given.

Third, the most frequent complication we encountered was a lesion or dysfunction of the chorda tympani nerve. It can be debated whether all these cases should be considered as a complication, especially since in at least a quarter of the cases the chorda was intentionally sacrificed to gain access to the cochlea and in only 22.5% of these cases there was a reported loss of taste for a prolonged period. Furthermore, loss or alteration of taste, decrease in tongue sensation or, less common, xerostomia are no longer present in 94% to 96% of patients where the chorda tympani nerve was cut, 2 years after surgery. Electro-gustometry thresholds, on the other hand, often remain elevated<sup>83,84</sup>, thus making it an unintended and unwanted event with permanent damage. Patients may also underreport persistent loss or alteration of taste and physicians may not always inquire about taste loss after surgery.

On the other hand, several authors included device failures in the total number of complications, which made the rate of actual medical complications lower.

The failure rate (hard and soft failure) in our series was 3.5%. This is comparable to the failure rate of 3.79% that was reported in a large multicenter study of 12,856 devices<sup>85</sup>. We found a decrease in device failures over the years, which is probably the result of

technological development. However, there may be some overestimation because the older devices have had a longer follow-up.

### 3.5. Conclusion

The benefits of using a database system were already acknowledged by Ray et al., who were the first to describe the use of a computerized database system for registering cochlear implant data<sup>86</sup>. The advantage of using the present database system is that it not only enables fast and accurate data entry, but also makes it easier to combine and compare results from different medical centers. This is particularly useful in comparing different surgical techniques and studying complications with a low incidence and high morbidity (such as meningitis). Therefore, we make this database freely available (database and manual can be downloaded at <http://bit.ly/cidatabasenijmegen>). Nevertheless, every complication registration system depends on consequent data entry by the surgeon or other members of the cochlear implant team.

In our series we found a relatively high number of complications in cochlear implant surgery that has been stable over the years, while the number of device failures has declined. This stresses the use of a uniform definition and classification system for complications in cochlear implant surgery, not only to fairly compare results but also for investigating means for reducing these complications.



### III | Complications and failures of cochlear implantation

#### 4. Clinical results and risk factors

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Risk factors for complications in cochlear implant surgery  
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Eur Arch Otorhinolaryngol. 2018 Epub ahead of print.



## Abstract

The objective of this study was to achieve uniform reporting of complications and failures in cochlear implantation, to analyze complications and failures and to identify risk factors for complications in a series of over 1,300 cochlear implantations. Data from all cochlear implantations from 1987 to 2015 were retrospectively and/or prospectively entered in a custom-made database. Complications were classified using the Clavien–Dindo system and risk factors were identified by statistical analysis. A complication rate of 18.4% and a device failure rate of 2.9% was found. There was a higher rate of hematoma in patients with a clotting disorder and when a subtotal petrosectomy was performed, a higher rate of wound infections in patients who were not vaccinated against *Streptococcus pneumoniae* and a higher rate of meningitis in patients with an inner ear malformation. The use of a strict definition of a medical complication and device failure - in combination with the Clavien-Dindo classification system - enables uniform and objective registration of adverse events and prevents any tendency to down-grade complications. Complication and failure rates in this series are comparable to those reported in literature. These results stress the need for pneumococcal vaccination, which may prevent general wound infections, but is especially important for patients with inner ear malformation, who have an increased risk of (postoperative) meningitis.

## 4.1. Introduction

Cochlear implantation is very successful in restoring hearing in patients with profound sensorineural hearing loss, but surgical complications are reported in 6-63% of the cases<sup>37-39,81,82</sup>. This complication rate is comparable to that of active middle ear implantation (16-21%<sup>87,88</sup>), but is higher than in other fields of otology such as cholesteatoma surgery (6-17%, although reports are sparse<sup>89,90</sup>).

The first step in reducing these complications is identification of the most common and most severe complications. Although there are many reports on complication rates, these results are hard to compare, since there is no consensus on reporting them (except for meningitis<sup>91</sup> and device failure<sup>92,93</sup>). Hansen et al. have proposed a useful overview of definitions and criteria, which was elaborated by Jeppesen et al.<sup>39,82</sup>, but unfortunately, this has not yet been widely used. Similar problems arise with classification: most studies differentiate between major and minor complications, but the use is inconsistent and a clear definition is rarely given. Hansen et al. have also addressed this problem, but their definition still leaves room for interpretation (e.g. 'a significant medical problem' is considered a major complication). To tackle this problem in general surgery, Clavien et al. developed a classification system (modified by Dindo et al), based on the therapy used to treat the complication.<sup>94,95</sup> Previously, the authors have used this Clavien-Dindo system, in combination with a custom-made database system, to classify complications in cochlear implant surgery.<sup>96</sup>

The second step is the identification of risk factors. In contrast to reports on complication rates, there are very few reports on this subject, mainly concerning meningitis<sup>97</sup> and wound infection.<sup>98,99</sup> Again, a uniform registration of complications is necessary in order to make a fair comparison between different treatment modalities. And especially since some (serious) complications are rare, this can only be achieved by pooling data from different studies.

The aim of this study was to not only give an overview of device failures and medical complications in over 1,300 cochlear implantations, but to also identify risk factors and find ways to reduce the number of complications.

## 4.2. Materials and methods

Data from all cochlear implantations between January 1<sup>st</sup> 1987 and January 1<sup>st</sup> 2015 were entered in a custom-made Microsoft Office Access (Redmond, Washington, USA) database (freely available: <http://bit.ly/cidatabasenijmegen>).<sup>96</sup> The majority of data were entered retrospectively from the patients' charts, but implantations and complications occurring after the start of the project were entered prospectively by members of the cochlear implant team. Patient demographics, pneumococcal vaccination status and possible risk

factors for complications (such as smoking, immunodeficiency/-suppression, clotting disorder/anticoagulant use and inner ear malformation) were registered. Implantation data such as the device type, primary/revision surgery, skin incision, surgical approach (posterior tympanotomy or subtotal petrosectomy), antibiotic prophylaxis and intra-operative findings (such as middle ear inflammation) were recorded.

The definition of a medical complication that was used, was based on the one provided by the Dutch Federation of Medical Specialists<sup>100</sup> and the recommendations of Jeppesen et al.<sup>39</sup>: *an unintended and unwanted event or condition during or following medical specialist treatment that is so detrimental for the health of the patient that adjustment of the medical treatment is necessary or that it causes irreversible damage; and is (probably) the result of, or has adverse consequences for the implantation.* A period of one year was considered a sufficient minimum follow-up time.

The consequences of a complication were registered in such a way, that both differentiation between ‘major’ (requiring additional surgery and/or hospitalization for treatment) and ‘minor’ complications was possible, and the use of the contracted form of the Clavien–Dindo classification system. This is a validated 5-scale classification system that is based on the treatment of the complication (Table 1).

**Table 1** Contracted form of the Clavien-Dindo classification of surgical complications<sup>95</sup>.

Grades	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Acceptable therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside.
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IV	Life-threatening complication (including CNS complications*) requiring IC/ICU-management
Grade V	Death of a patient
Suffix ‘d’	If the patient suffers from a complication at the time of discharge, the suffix “d” (for ‘disability’) is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication.

\* brain hemorrhage, ischemic stroke, subarachnoidal bleeding, but excluding transient ischemic attacks; CNS: central nervous system; IC: Intermediate care; ICU: Intensive care unit

The definition of a device failure was based on the European consensus on implant failures<sup>93</sup> and the soft failures consensus<sup>92</sup>: *hard failure is a device with characteristics outside the manufacturer’s specification resulting in a loss of clinical benefit and soft failure is a device with characteristics within the manufacturer’s specification, but with unexplained declining performance or the occurrence of (non)auditory aversive symptoms such as atypical tinnitus, facial nerve stimulation or a popping or shocking sensation.*

Pearson’s chi-square test was used to test the relationship between possible risk factors and the occurrence of certain complications. If multiple risk factors were tested for one complication, a loglinear analysis was done instead. If the number of events was small, Fisher’s exact test was used, with a Bonferroni correction to adjust the p-value used as criterion for significance. IBM SPSS Statistics version 22.0 (Armonk, New York, USA) was used for all analyses.

### 4.3. Results

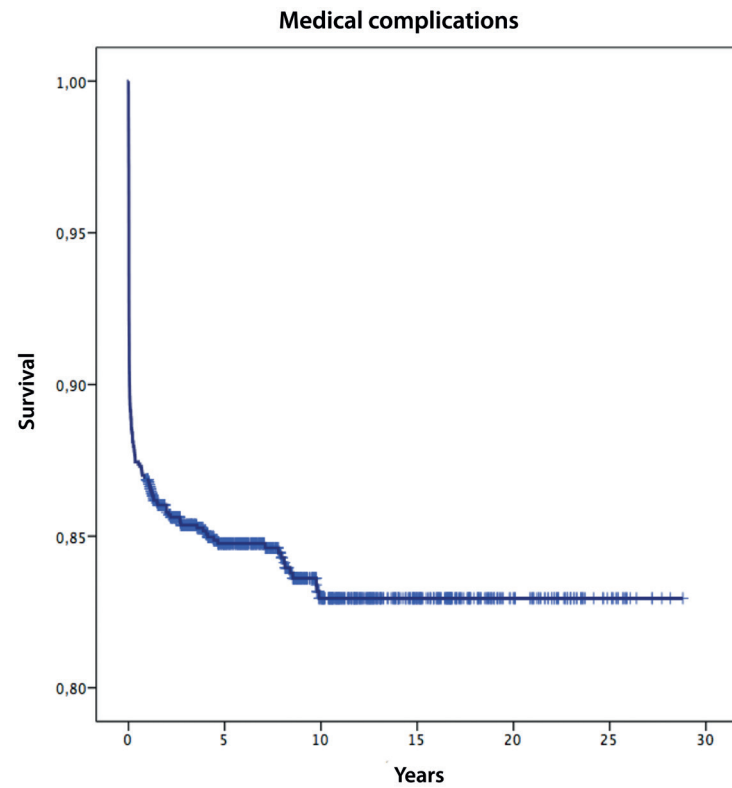
#### Population

The first cochlear implantation in Nijmegen, the Netherlands, took place in 1987. Up to 2015, 1222 patients (656 women and 566 men) underwent a total of 1362 implantations (527 in children and 835 in adults). Mean age at implantation was 34.8 years (range, 0.6–87.6 years). Mean follow-up time was 7.9 years (range, 0.1–27.2 years; follow-up time for some implantations was less than one year because of device failure or patients lost to follow-up).

#### Complications

In 18.4% of the implantations (n=250), 1 or more complications were registered. In 224 cases (16.4%) there was a single complication during or after implantation and in 26 cases (1.9 %) there were 2 complications; 276 complications in total. Forty-three (15.6%) of these complications occurred intra-operatively and 233 (84.4%) occurred post-operatively. Fifty-seven (20.6%) of these complications were classified as ‘major’ and 219 (79.3%) as ‘minor’. Table 2 displays the total list of complications, classified by the Clavien–Dindo system. The only patient with a grade IV complication had a preexistent metabolic disorder and lactate acidosis that required ICU management. The category ‘other’ ranged from external otitis to urinary retention and delirium.

The majority of postoperative complications (83.6%) occurred within 1 year after surgery (Fig. 1). Medical complications were equally common in adults as in children (18.2 vs. 18.6% respectively, Pearson Chi<sup>2</sup>, p = 0.057).



**Figure 1** Kaplan-Meier estimated survival function for medical complications.

### Chorda tympani lesion/dysfunction

Ten patients reported taste disorder after surgery while the chorda tympani nerve was left macroscopically intact during surgery. In contrast, of the 34 patients in which the nerve was cut, only 4 patients reported taste disorder. In 19 of these patients, the chorda was cut intentionally. Overall, only 3 patients reported taste disorder several weeks after surgery (subsequent data were often unavailable).

### Seroma

The majority of patients with seroma were treated by puncture aspiration and/or pressure bandage (one puncture was performed under general anesthesia), and some received additional antibiotics. There was no relationship between the occurrence of seroma and the type of skin incision, nor with the surgical approach. Seroma was more common in patients who smoked (6.1 vs. 2.3%), but the difference was not significant (Fisher's exact test,  $p = 0.027$ ).

**Table 2** Total list of complications, classified by the Clavien–Dindo system.

Complication	Clavien-Dindo grade				Frequency	Percent	Incidence
	I	II	III	IV			
Chorda tympani lesion/dysfunction	44 (3)				44	15.9	3.2
Wound infection		35 (0)	7 (0)		42	15.2	3.1
Seroma	25 (0)	11 (0)	1 (0)		37	13.4	2.7
Pain	18 (4)	9 (2)	5 (2)		32	11.6	2.3
Hematoma	10 (0)	5 (0)	1 (0)		16	5.8	1.2
Traumatic/pressure skin lesion	5 (0)	8 (0)	1 (0)		14	5.1	1.0
Vertigo	8 (4)	4 (1)			12	4.3	0.9
Mastoiditis		5 (0)	4 (0)		9	3.3	0.7
CSF leak		3 (0)	1 (0)		4	1.4	0.3
Skin flap problems		2 (0)	2 (0)		4	1.4	0.3
Electrode extrusion			4 (0)		4	1.4	0.3
Meningitis		3 (0)			3	1.1	0.2
Misplaced electrode array			3 (0)		3	1.1	0.2
Tinnitus	3 (2)				3	1.1	0.2
Facial nerve lesion/dysfunction		1 (0)	1 (0)		2	0.7	0.1
Magnet displacement			2 (0)		2	0.7	0.1
Electrode array dislocation			1 (0)		1	0.4	0.1
Other	10 (0)	31 (2)	2 (0)	1 (0)	44	15.9	3.2
<b>Total</b>	<b>123 (13)</b>	<b>117 (5)</b>	<b>34 (2)</b>	<b>1 (0)</b>	<b>276</b>	<b>100.0</b>	<b>NA</b>

Data represent  $n$  unless indicated otherwise; values in brackets represent numbers of cases with suffix 'd' (for disability). CSF: cerebrospinal fluid; NA: not applicable.

### Hematoma

Hematomas were treated in the same manner as seromas. No association was found between the occurrence of hematoma and the type of skin incision, but hematoma (at the primary surgical site) was significantly more common when subtotal petrosectomy was performed (in patients with a radical cavity,  $n=15$ ), compared to posterior tympanotomy (13.3 vs. 1.0%, Fisher's exact test,  $p = 0.011$ ). It occurred more often in patients with cardiovascular disease (3.4 vs. 0.9%), but this difference was not significant (Fisher's exact test,  $p = 0.066$ ). A significant correlation was found between the presence of clotting disorder or anticoagulant use, and hematoma: 5.1 vs. 0.9% (Fisher's exact test,  $p = 0.009$ ).

### Pain

Chronic postoperative pain was more commonly found in recent years (not reported before 2004), but no correlation was found with the type of skin incision or device that was used. Nor did it matter whether it was primary or revision surgery. It was mostly treated with general or local anesthetics.

### Wound infection

The majority of wound infections presented as superficial inflammation of the skin and were treated with oral antibiotics. There were 10 cases of major wound infection, 1 had a concurrent acute otitis media (mean time to infection was 60.7 days [range, 7-426 days]). Three of these patients were treated with intravenous antibiotics and the rest required surgical intervention, resulting in explantation in 4 cases. In one patient, the implant was preserved with the use of gentamicin-impregnated collagen sponges.<sup>101</sup> No relationship was found between the duration of antibiotic administration (intraoperative, intra- and 1-7 days postoperative or intra- and 8-14 days postoperative) and the occurrence of wound infections. An association with immunodeficiency/-suppression or middle ear inflammation (including otitis media with effusion) during surgery was neither found, but there was a significantly higher rate of wound infections in patients who were not vaccinated against *Streptococcus pneumoniae* (5.7 vs. 2.6%, loglinear partial  $\chi^2$ ,  $p = 0.031$ ).

### Meningitis

There were 3 cases of postoperative meningitis, occurring 0, 391 and 800 days after implantation. One case had a *Pseudomonas aeruginosa* infection and 2 had a *Streptococcus pneumoniae* infection. Of the latter, 1 patient had recurrent meningitis before implantation and had been vaccinated against *Streptococcus pneumoniae*, but later proved to have a specific antibody deficiency (the other patient had not been vaccinated at the time of meningitis). Two of the patients had an inner ear malformation: one patient had an incomplete partition type II (with a gusher during surgery) and the other an isolated enlarged internal auditory canal.

Despite the low frequency of meningitis, an attempt was made to identify risk factors. No relationship between vaccination against *Streptococcus pneumoniae*, immunodeficiency/-suppression (total  $n=12$ ) and the occurrence of meningitis was found. Nor did there prove to be a relationship between middle ear inflammation at the time of implantation (total  $n=66$ ) and meningitis (1.5 vs. 0.2%, Fisher's exact test,  $p = 0.139$ ). There was, however, a significant association between inner ear malformation (total  $n=87$ ) and the occurrence of meningitis (2.3 vs. 0.1%, Fisher's exact,  $p = 0.012$ ).

### Facial nerve lesion

One patient had a transient facial nerve dysfunction (House-Brackmann grade III) 19 days after surgery. He was treated with prednisone and famciclovir and fully recovered. A 4-year-old child with obliterated cochleae had a facial nerve paresis directly after surgery (House-Brackmann grade III). She underwent revision surgery and the electrode array proved to be in contact with a dehiscence part of the facial nerve. It was lifted of the nerve and fixated, resulting in full recovery of symptoms.

### Device failures

There were 40 cases of device failure (2.9%): 27 cases of hard failure (2.0%) and 13 cases of soft failure (1.0%). Failures per device type are listed in table 3. The mean time to device failure was 5.4 years. The majority of soft failures consisted of facial nerve stimulation ( $n=7$ ): one patient was reimplanted, one was implanted in the other ear, one became a non-user and in the other patients the mapping had to be significantly adjusted. Facial nerve stimulation was significantly more common in patients with otosclerosis (total  $n=36$ ; 5.6 vs. 0.4%, Fisher's exact test,  $p = 0.013$ ). Three patients experienced a decline in performance (2 were reimplanted and 1 was implanted in the other ear) and 3 patients experienced pain only when using the implant (1 was explanted, in 1 case the tympanic nerve was cut [resulting in minimal improvement] and in the other case the patient mainly used his other CI).

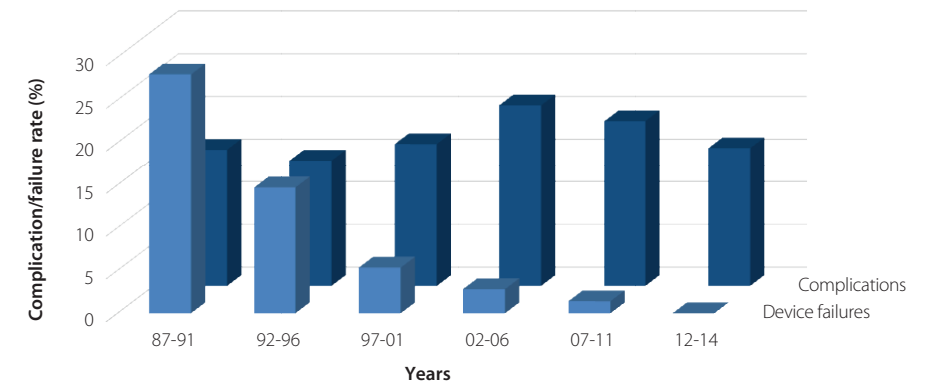
### Explantations

Forty-seven patients (3.5%) underwent explantation of their CI. In the majority of cases ( $n=31$ ), this was because of device failure (4 soft failures and 27 hard failures). Two patients who initially received a 3M/House or Vienna device were reimplanted with a multichannel device and two other patients requested explantation because of poor functional outcome. Twelve patients underwent explantation because of a medical complication: 6 patients had a wound infection or dehiscence, 1 had a complicated posttraumatic CSF leak, there were 3 cases of dislocation of the electrode array and 2 patients had a misplaced electrode array (1 in hypotympanum and 1 tip-foldover).

**Table 3** Device failures per device type.

Device type	N	Device failures (%)	Mean follow-up (years)
3M/House	1	0 (0)	11.0
3M/Vienna	9	3 (33.3)	17.2
CII with HiFocus I electrode, no positioner	3	0 (0)	12.7
CII with HiFocus II electrode	8	0 (0)	13.5
CII with HiFocus II electrode, no positioner	7	0 (0)	11.1
Clarion 1.2 with Enhanced bipolar electrode	24	3 (12.5)	15.2
Clarion 1.2 with HiFocus I electrode	12	2 (16.7)	11.7
Combi40+ with Split electrode	1	0 (0)	2.1
Combi40+ with Standard electrode	3	3 (100)	1.1
ConcertoMi1000 with Flex28 electrode	1	0 (0)	3.9
ConcertoMi1000 with FlexSoft electrode	6	0 (0)	4.1
HiRes 90K Advantage with HiFocus 1j electrode	6	0 (0)	1.9
HiRes 90K Advantage with Midscala electrode	29	0 (0)	1.9
HiRes 90K with HiFocus 1j electrode	73	5 (6.8)	5.7
HiRes 90K with HiFocus Helix electrode	50	1 (2)	8.2
Laura	5	5 (100)	7.0
Nucleus 20+2L	16	1 (6.3)	19.3
Nucleus 24	75	2 (2.7)	15.5
Nucleus 24 with Contour Advance electrode	105	3 (2.9)	9.9
Nucleus 24 with Contour electrode	70	0 (0)	12.5
Nucleus 24 with Double Array electrode	5	0 (0)	8.5
Nucleus 24k	14	0 (0)	14.9
Nucleus 422 with Slim Straight electrode	69	0 (0)	2.2
Nucleus 512 with Contour Advance electrode	121	2 (1.7)	4.5
Nucleus Freedom with Contour Advance electrode	542	4 (0.7)	5.6
Nucleus Freedom with Hybrid-L24 electrode	5	0 (0)	7.8
Nucleus Freedom with Straight electrode	4	0 (0)	5.0
Nucleus Mini System 22	62	6 (9.7)	20.2
SonataTi100 with Flex28 electrode	3	0 (0)	3.7
SonataTi100 with FlexEAS electrode	11	0 (0)	6.7
SonataTi100 with Medium electrode	18	0 (0)	2.7
Synchrony with Medium electrode	4	0 (0)	1.1
Total	1362	40 (2.9)	7.9

Complication and device failure rates per five years are displayed in Fig. 2. A significant decrease in device failures was found over the years (chi-square (5 degrees of freedom) = 105.50,  $p < 0.001$ ), while the incidence of medical complications remained fairly constant (no significant difference between five-year periods).

**Figure 2** Complication and device failure rates per five years.

#### 4.4. Discussion

In this series of 1362 cochlear implantations, a complication rate of 18.4% and a device failure rate of 2.9% was found. There is a large variation of reported complication rates in literature.<sup>37-39,81,82</sup> Important factors are the definition of a complication that is used, the difference between retro- or prospective data collection, and whether or not to consider the (intentionally) cutting of the chorda tympani nerve and a device failure a medical complication.<sup>96</sup> Use of the Clavien-Dindo classification system and the aforementioned strict definition of a complication prevents subjective interpretation of adverse events and any tendency to down-grade complications, because it is based on data that are usually well documented.<sup>102</sup>

The main goal of this study was to identify risk factors for medical complications. Probably the best-known publication on this subject is by Reefhuis et al., who demonstrated that the use of an implant with a positioner in children was strongly associated with post-implantation bacterial meningitis, resulting in the disuse of separate positioners. They also demonstrated that the joint presence of radiographic evidence of inner ear malformation and a cerebrospinal fluid leak was associated with an increased risk of postoperative meningitis, and the presence of a cerebrospinal fluid leak alone with an increased risk of perioperative meningitis ( $\leq 30$  days after surgery).<sup>97</sup> Despite the lower number of implantations and cases of meningitis in this series, this is the first study to demonstrate inner ear malformation alone as a risk factor for postoperative meningitis, although numerous case reports have noted the association between inner ear malformation and meningitis (without cochlear implantation).<sup>103</sup> Loundon et al. also reported a significantly higher overall complication rate (including a misplaced electrode array, meningitis and

persistent CSF leak) in children with inner ear malformation, than found in the rest of their population.<sup>38</sup>

In general surgery, risk factors associated with wound infections include co-morbidities (such as diabetes), advanced age, risk indices, patient frailty, longer surgeries and surgery complexity.<sup>104</sup> In cochlear implantation, both a chronic health condition and a history of chronic ear disease have been suggested (but not statistically proven) as risk factors for postoperative infection.<sup>98,99</sup> In this series, no association with immunodeficiency/-suppression or middle ear inflammation at the time of surgery was found. There is insufficient evidence on the effects of perioperative antibiotics on risk of infections after cochlear implantation.<sup>105</sup> A relationship between the duration of antibiotic use and wound infections was neither found in this study, but this may be obscured by the fact that the majority of data was obtained retrospectively and no intention to treat analysis could be performed. Little is known about the bacterial flora in wound infections after cochlear implantation, or ear surgery in general. Although a negative association between *Streptococcus pneumoniae* vaccination and wound infections was found, a study on bacterial flora on explanted CIs did not show the presence of *Streptococcus pneumoniae*<sup>106</sup>, so the clinical relevance of this finding is unclear.

Other risk factors that were identified concerned hematoma: this was more common when a subtotal petrosectomy was performed (possibly due to the temporalis muscle flap) and in patients with a clotting disorder or anticoagulant use. Two previous studies found that coagulation disorders and incision type are predisposing factors for hematoma.<sup>107,108</sup> Risk factors for seromas or postoperative chronic pain could not be identified.

Middle ear inflammation (including otitis media with effusion) was not found to be a risk factor for postoperative wound infection or meningitis, although bleeding and swelling of the middle ear mucosa may make surgery more challenging. Insertion of a ventilation tube does not seem to be required in these cases.<sup>109</sup>

Chorda tympani lesion/dysfunction was the most common complication. While few of these patients suffer from persistent taste disorder, thresholds on electrogustometry often remain elevated.<sup>110</sup> Furthermore, the low number of patients with taste disorder after cutting of the nerve may be due to under-reporting, because patients are not always questioned on this subject postoperatively.

The incidence of medical complications was stable over the years. This does not mean that there is no learning curve in cochlear implantation (the implantations were done by surgeons with different amounts of experience and functional results were not included), but the efforts to reduce complications such as wound infections and seromas by reducing OR door swings and adjusting incision types and antibiotic regimens, seem to have borne little fruit. The number of device failures on the other hand, has decreased significantly over the years. This may partially be explained by the duration of follow-up, but since the mean time to device failure was 5.4 years, this is probably mainly due to

technological advancement. The failure rate of 2.9% in this series was somewhat lower than the 3.8% that was reported in a large multicenter study.<sup>111</sup>

## 4.5. Conclusion

Risk factors identified in this study may give some leads to reduce the number of complications in the future. Unfortunately, no risk factors were identified for common complications such as seroma and chronic pain. To determine the effect of factors such as prophylactic antibiotics, prospective trials are necessary (which is the third step in reducing complications). Because a higher rate of hematomas in patients with coagulation disorders and in implantation combined with subtotal petrosectomy was found, more attention to hemostasis is necessary in these patients (although most were grade I complications). Above all, this study stresses the need for pneumococcal vaccination, which may prevent general wound infections, but is especially important for patients with inner ear malformation, who have an increased risk of (postoperative) meningitis. Further precautions in these cases include a fibrous tissue seal around the electrode array at the cochleostomy site, and treatment of postoperative acute otitis media according to the protocol proposed by Rubin et al.<sup>112,113</sup> Overall, cochlear implantation is a very successful and safe procedure with a limited number of serious complications, but the relative high number of minor complications still leaves room for improvement.

### III | Complications and failures of cochlear implantation

#### 5. Gentamicin-impregnated collagen sponges for the treatment of infections

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The use of gentamicin-impregnated collagen sponges (Garacol®/Duracoll®) in cochlear implant infections: our experience in four cases.

Buijs EF, Theunisse HJ, Mulder JJ, van den Hoogen FJ, Offeciers EF, Zarowski AJ, Mylanus EA. Clin Otolaryngol. 2015 Oct;40(5):492-5.





## Abstract

Cochlear implantation has an overall infection incidence of 0.4–5.2%. Major infectious complications often require device explantation. Gentamicin sponges may halt the infection through high local concentrations at the surgical site. This technique may reduce the need of device explantation and may lead to a possible cost reduction. Salvage surgery with gentamicin sponges was attempted in four patients with severe soft tissue infection after cochlear implantation. This was successful in two of four cases. Larger studies are needed to fully understand the effectiveness.

## 5.1. Introduction

Cochlear implantation is a treatment for deafness and severe sensorineural hearing loss in pediatric and adult patients. Cochlear implants (CIs) bypass damaged or missing hair cells in the cochlea by directly stimulating auditory nerve fibers, allowing for speech perception in most users.

Although very successful in most cases, the incidence of medical complications is somewhere between 6 and 63%<sup>37-39,81,82</sup>. These complications can be classified as minor or major complications. Minor complications are treated expectantly and/or with medication alone, while major complications require additional surgery and/or hospitalisation<sup>81</sup>. The incidence of major complications in cochlear implantation has been reported to be 3.2–8.6%, with an overall incidence of infections of 0.4–5.2%<sup>37,39,81,96,98,114</sup>. General risk factors for wound infection are comorbidities (e.g. diabetes, chronic obstructive pulmonary disease and cardiovascular disease), increasing age and BMI, and complexity and/or duration of surgery<sup>104</sup>. For cochlear implantation specifically, a history of ear infections is a significant risk factor for postoperative infection<sup>98</sup>. When major infectious complications occur, the main treatment is surgical intervention and often device explantation, especially in cases with device exposure<sup>81,98</sup>. The management of these wound infections is complex, mainly because of the presence of biofilm, resulting in a reduced metabolic activity at the surgical site and a reduced effect of many antimicrobial agents<sup>115</sup>.

Implantable gentamicin-impregnated collagen sponges such as Garacol®/Duracoll® have been popularized in recent years to prevent surgical site infections. We hereby report the results of the use of gentamicin sponges in salvage surgery for severe soft tissue infection after cochlear implantation in both pediatric and adult patients.

## 5.2. Materials and methods

Four consecutive patients, who presented with severe wound infection after cochlear implantation (CIs of Cochlear®, Sydney, Australia and Advanced Bionics, Stäfa, Switzerland) in two clinics in Antwerp, Belgium and Nijmegen, the Netherlands, were included in this study. After full understanding of the aim and consent given for the treatment, three male patients and one female patient participated in this study. Age ranged from 2 to 80 years.

### Surgical technique

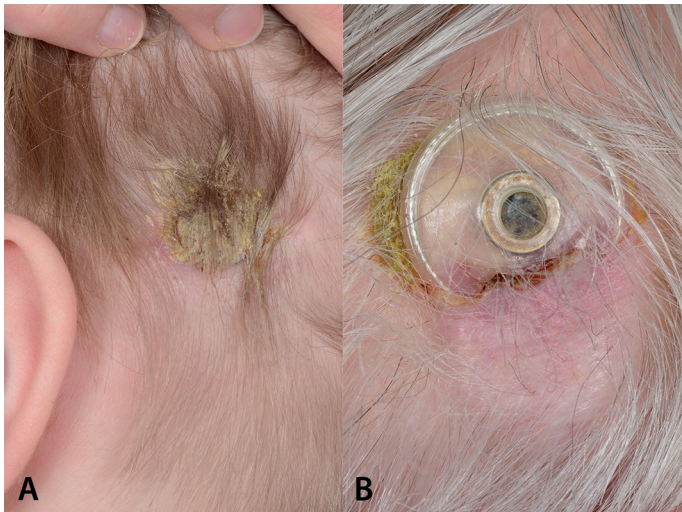
All patients underwent salvage surgery in an attempt to resolve the infection and preserve the implant. Patients received antibiotic prophylaxis (cefazolin and metronidazole) 30 min before salvage surgery. The procedure consisted of a retro-auricular incision along the previous scar and removal of the infected skin. After thorough inspection and removal of granulation tissue, a new bed for the receiver and electrode was drilled. Garacol®

(the Netherlands) or Duracoll® (Belgium) gentamicin sponges (both of EUSA Pharma, Hemel Hempstead, UK) were placed in the newly drilled bed and, after the implant was placed in the bed, on top of the implant. Closure in two layers and a pressure dressing was applied. Postoperatively, patients were treated with antibiotics based on the available microbiological cultures.

5.3. Results

Of four patients included in our study, two patients had developed an early postoperative infection (<30 days) a week after cochlear implantation. Two patients had developed a delayed postoperative infection (>30 days) 3 months and 50 months after surgery. In two of four patients, the infection resolved completely. Follow-up ranged from 13 to 27 months after salvage surgery (Table 1).

The first patient had no risk factors for wound infection. Three months after implantation, the wound became dehiscent (Fig. 1A). Despite salvage surgery with gentamicin sponges 3 months later, the infection persisted and the device was removed. Our second patient had a history of frequent otitis. More than three years after cochlear implantation, there was extrusion of the device (Fig. 1B). After 2 months of conservative treatment, salvage surgery was performed. Twelve months after surgery, there was again



**Figure 1** Wound dehiscence in patient 1 (A) and extrusion of the cochlear implant in patient 2 (B).

**Table 1** Summary of patient characteristics and treatment.

Patient	Age*	Sex	Infection **	Pre op swab	Salvage surgery **	Surgery swab	Post op treatment	Complications***
1	2,6	M	3 months	-	6 months	No pathogen found	Amoxicillin/clavulanate 4 weeks	CI lost after 2,5 months
2	80,3	F	50 months	-	52 months	<i>Staphylococcus lugdunensis</i>	Amoxicillin/clavulanate 1 week	Reinfection <i>Proteus mirabilis</i> CI lost after 1 year, 3 months
3	61,1	M	7 days	<i>Enterobacter cloacae</i> <i>Staphylococcus aureus</i>	10 days	<i>Enterobacter cloacae</i> , <i>Staphylococcus aureus</i> , <i>Serratia marcescens</i>	Clindamycin and Ciprofloxacin 6 weeks	No
4	42,7	M	7 days	<i>Pseudomonas aeruginosa</i>	2 months, 7 days	-	Ceftazidime 2 weeks	No

\* Age at implant (years, months), \*\* Time after implantation, \*\*\* Time after salvage surgery.

extrusion of the device and surgical removal was performed. The third patient had a history of progressive bilateral hearing loss due to otosclerosis. A week after cochlear implantation, the patient presented with fever and drainage of pus from the retro-auricular wound. Three days later, salvage surgery with gentamicin sponges was performed. After 27 months of follow-up, no complications were seen. Our fourth patient had a history of insulin dependent diabetes and a probable hereditary progressive hearing loss since 15 years. Seven days after implantation, the wound became dehiscent. The wound was treated with debridement and long-term antibiotics (tobramycin 3 days, intravenous ceftazidime 6 g/day for 6 weeks). This treatment was insufficient and salvage surgery was performed 2 months later. Ceftazidime was continued for 2 weeks after the surgery. After a 13 month follow-up, no complications were seen.

## 5.4. Discussion

There is no standardized treatment for surgical wound infection after cochlear implantation. Although mild infections may be treated with antibiotics alone, device explantation in severe infections is often considered the only treatment option to halt the infection<sup>81,98</sup>. The use of local gentamicin to treat the infection could be effective in preserving the device, as shown in two of four patients in this study.

### Effectiveness and safety

The time after surgery to develop soft tissue infection varied among our patients in this study. Two patients with an early postoperative infection showed good response to the salvage surgery with gentamicin sponges. In contrast, two patients with a delayed infection, 3 and 5 months after surgery, did not have this positive outcome. It might be that the local application of gentamicin is more effective in short onset infections after implantation, as shown in our results. This may be because long-term infections can be so advanced that treatment with local application is ineffective to control the process, or because these infections have a different etiology. It is reported that wound infections with device exposure require device removal in 89% of the cases despite prolonged antibiotic treatment<sup>98</sup>, and this may also apply to salvage surgery with gentamicin sponges. To fully understand this, larger study groups are needed.

Antonelli et al.<sup>106</sup> recently studied pathogens in both infectious and non-infectious explanted CIs. In infectious CIs, *Staphylococcus aureus* was found significantly more often. *Pseudomonas aeruginosa* was also more common in the infected specimens but without significance. Our study also found these pathogens among the cultures of pre- and peroperative swabs, all sensitive to gentamicin treatment (Table 1).

Aminoglycosides such as gentamicin are known to have a small therapeutic index. Local application of antibiotics, such as powder or sponges, can be used to achieve high

tissue concentrations with lower risk of systemic toxicity. After implantation of a gentamicin collagen sponge (containing up to 130 mg gentamicin sulphate per sponge), within 24 h the concentration at the surgical site can reach concentrations up to 170 lg/mL. After 24 h, concentrations drop to an average of 10 lg/mL lasting up to 10 days, well above the minimum inhibitory concentration of 4–8 lg/mL for gentamicin-sensitive pathogens. Within 24 h, the systemic concentration drops below 2 lg/mL, well below the toxicity threshold<sup>116</sup>. The use of gentamicin absorbable sponges is considered safe with high, bactericidal concentrations at the surgical site without high systemic concentrations. The sponges are fully biocompatible and biodegradable and therefore do not have to be removed.

### Comparison with other studies

Few reports have described the use of gentamicin sponges for wound infections in CIs<sup>39,117</sup>. Jeppesen et al.<sup>39</sup> reported one case of successful treatment of soft tissue infection in CI with a gentamicin sponge (Gentacoll®) and intravenous cefuroxime. A recent study evaluated the effectiveness and safety of gentamicin sponges in soft tissue infections in pediatric CIs. In all three patients, the infection resolved after salvage surgery using Collatamp® sponges with a follow-up of 12 months<sup>117</sup>. These infections consisted of serous fluid collections or hematoma without device exposure and therefore may be considered milder infections than our cases. Because one of our patients again developed device extrusion 12 months after salvage surgery, a 12-month follow-up period may be too short (follow-up in our series ranged from 13 to 27 months).

There are multiple benefits in preserving implants. Aside from the emotional benefit for the patient, preserving the implant could possibly reduce costs. According to the Dutch Ministry of Health, Welfare and Sport, the standardized cost of the implantation of a single cochlear implant is estimated to be € 42.527. The gentamicin collagen sponges we used have an estimated price of € 170 per sponge measuring 10 x 10 cm, a small fraction of the price of a CI implantation we also expect it to be in other European countries. Therefore, besides that it might save the patient an extra procedure, salvage surgery with gentamicin sponges may lead to significant cost savings, even if only half of the implants are preserved.

## 5.5. Conclusion

We demonstrated that salvage surgery with gentamicin sponges is a safe technique that might prevent device explantation in severe soft tissue infection. This was successful in two of four cases in our series, all in early postoperative infections without extensive device exposure. The use of gentamicin sponges results in high concentrations of gentamicin at the surgical site while minimizing the risk of systemic toxicity, without the need of removal of the sponge.

This relatively low-risk procedure may not only be beneficial for the patient but may also lead to a significant cost reduction. This technique seems very promising and larger future studies are needed to fully investigate the effectiveness of this local application in CIs.

## IV | Surgical planning and evaluation of cochlear nerve implantation

### 6. The transcochlear approach

**Published as:**

Surgical planning and evaluation of implanting a penetrating cochlear nerve implant in human temporal bones using microcomputed tomography.

Theunisse HJ, Gotthardt M, Mylanus EA.

Otol Neurotol. 2012 Aug;33(6):1027-33



## Abstract

The objective of this study was to develop a transmastoid-posterior tympanotomy approach for the implantation of a penetrating auditory prosthesis in the most distal portion of the cochlear nerve. Animal studies suggest that penetrating cochlear nerve implants may overcome limitations of current cochlear implant systems. One step towards human implantation is the development of a suitable surgical approach. In computer rendered 3D models (based on micro-CT scans of 10 human temporal bones), we simulated trajectories through the most basal part of the cochlea that gave access to the most distal portion of the cochlear nerve with minimal damage to intracochlear structures. We determined their vectors with respect to the mid-modiolar axis and posterior round window edge and assessed if they intersected the chorda tympani nerve. The typical vector obtained with these 3D models ran in an anterosuperior direction, through the inferior part of the facial recess and anterior round window edge. In 7 out of 10 temporal bones, this trajectory intersected the chorda tympani nerve. Based on the vectors, dummy probes were implanted in 3 out of 10 temporal bones and the need for chorda tympani removal was confirmed in accordance with the 3D models. Postoperative micro-CT scans revealed that all probes were successfully implanted in the cochlear nerve while the osseous spiral lamina and basilar membrane were preserved. The vector for drilling and implantation found in this study can be used as a guideline for real-life surgery and therefore is another step towards the clinical implementation of cochlear nerve implants.

## 6.1. Introduction

The first implanted electrical neural stimulator to restore hearing used a wire electrode implanted directly in the cochlear nerve <sup>118</sup>. In following years, while Simmons reported promising results in patients implanted with wire electrodes in the modiolar nerve <sup>119</sup>, House began his work on implanting wire electrodes in the scala tympani (ST), which eventually led to the development of modern cochlear implants <sup>120</sup>. The main reasons to favor the ST over the modiolar arrays were the relatively easy surgical access to the ST, the straightforward tonotopic organization of the scala and the fear of damaging fibers of the cochlear nerve during the surgical procedure of implanting a relatively large electrode array into it. There are, however, several good reasons to revisit the concept of intraneural stimulation.

Directly stimulating the nerve fibers results in (a) lower energy requirements, (b) higher spatial selectivity, and (c) decreased chance of stimulating the facial nerve, a complication that is especially common in patients with otosclerosis <sup>121</sup>. Since the cochlear nerve has a tonotopic organization in accordance to the cochlea, it is possible to represent the lower frequencies as the array can reach fibers originating from the cochlear apex (which is difficult with intrascalar arrays).

With the development of microelectrode arrays (which allow less traumatic insertion and more selective stimulation), several of these advantages were confirmed in animal studies. Implantation of various types of these arrays in the cochlear nerve of guinea pigs and cats led to up to 50-fold lower stimulation thresholds and a higher specificity of stimulation than with intrascalar stimulation <sup>122, 123, 124, 125</sup>. Middlebrooks et al. additionally reported wider dynamic ranges and the successful stimulation of lower-frequency fibers <sup>125</sup>.

Although results are promising, several issues have to be resolved for the development of a practical auditory prosthetic device that can equal the results of cochlear implants.

We believe that the site most suitable for intraneural implantation is the distal end of the cochlear nerve. Just proximal to the lamina cribrosa, the cochlear nerve is separated from the facial and vestibular nerves (thereby reducing the risk of stimulation of these nerves) and nerve movement is limited by its fixation to the cochlea.

Given otologic surgeons experience with posterior tympanotomy techniques in cochlear implantation, a modification of this procedure is a plausible surgical approach to reach the modiolar trunk. This approach is also a common technique used in animal studies on intraneural implantation where after the posterior tympanotomy, the round window (RW) is enlarged and the underlying modiolar wall is opened to expose the nerve. There are very few publications that discuss this approach in humans.

Our aim was to investigate the suitability of a transcochlear surgical approach to the cochlear nerve while preserving intracochlear structures by using 3D models of human temporal bones (TBs). By implanting dummy probes into some of these TBs, we aimed to evaluate if our surgical planning was feasible.

## 6.2. Materials and methods

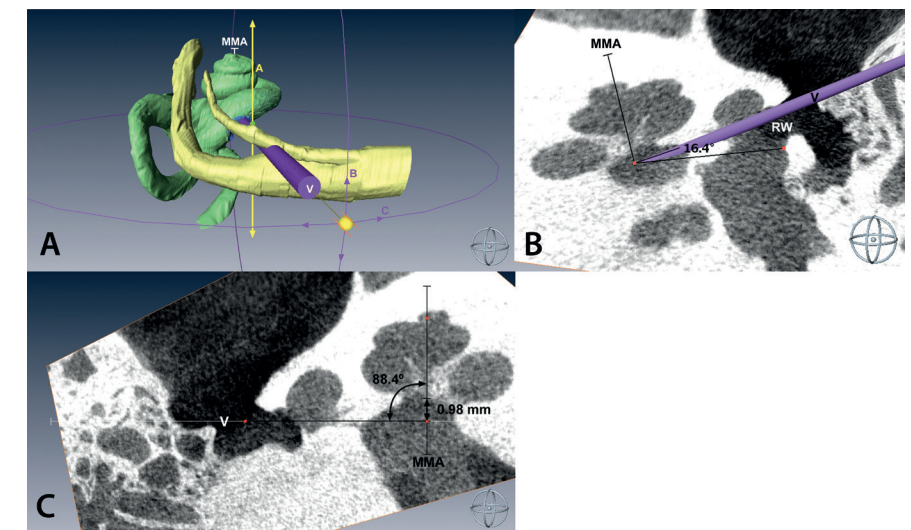
The CT device of an Inveon™ small-animal PET/CT system (Siemens Healthcare, Erlangen, Germany) was used to acquire micro-CT scans of ten formalin-fixed human TBs. As the field of view of the acquisition protocol for the preoperative evaluation was 41 x 61 mm, the TBs were cut to a cylindrical shape to fit this volume. Care was taken to ensure that all anatomical landmarks that could limit the surgical approach (such as the sigmoid sinus) were included in the specimen. The protocol consisted of the following settings: X-ray source voltage: 80 kV; X-ray source current: 500 mA; exposure time: 1000 ms; rotation: 202°; and steps: 202. This resulted in reconstructed image files with a voxel size of 0.04 mm. For the visualization of soft tissues and the implanted probes, we used an acquisition protocol with a higher magnification (field of view of 32 x 21 mm), more rotational steps (360°, 720 steps) and a voxel size of 0.01 mm.

We applied a similar method as used by Meshik et al. (to analyze cochlear implant insertion vectors)<sup>126</sup> to create 3D models of the TBs. Using AMIRA imaging software (Visage Imaging, Carlsbad, USA), we rendered two surface models of each TB: one of the high resolution micro-CT scan of the basal turn, and one of the normal resolution scan of the complete bony labyrinth and facial nerve. These two models were fused to create one model that contained all the structures that were relevant for our surgical planning (osseous spiral lamina [OSL], cochlear nerve, etc.). Using a multiplanar reconstruction tool, we selected the mid-modiolar axis (MMA) in these models. We then created a cylindrical shaped object with a diameter of 0.8 mm and a length of 20.0 mm to act as an implantation vector. We chose this diameter because the height of the ST in the first half of the basal turn decreases from approximately 1.25 mm to 1.03 mm<sup>127,128</sup>, the vector would probably not run fully perpendicular to the OSL and we aimed to preserve the veins located on the floor of the scala (because we believe that destruction of these veins, which drain the spiral ganglion and external walls of the scala tympani and media, might negatively affect these structures and lead to entry of blood into the scala tympani)<sup>129, 130</sup>. Next, we attempted to fit this implant vector into the surface model based on six formulated criterions applied in the following order (the first being the most important):

- The vector had to run between the facial nerve and the annulus fibrosis tympanicus (consistent with the posterior tympanotomy approach);
- The vector had to run through the MMA at the level of the cochlear nerve, representing the center of the nerve and location of the low-frequency fibers;
- The vector had to run as far to the basal end of the ST as possible, sacrificing only the highest frequency spiral ganglion cells (which have little clinical relevance because they fall outside the frequency range of speech) and giving the highest chance of survival for the chorda tympani nerve (CTN);

- The vector had to run medial from the OSL/basilar membrane (at the scala tympani side) to prevent opening the scala media;
- The vector had to run through separate openings in the lateral and medial cochlear wall to preserve the scalar floor;
- The vector had to run through the most distal portion of the nerve as possible, where it is fixed to the base of the cochlea and separated from the facial nerve by the falciform crest.

The optimal position of the vector was acquired by manual translation along and rotation around a point on the MMA (Fig. 1a). For instance, the vector was positioned as far to the basal end of the ST by rotating it around the MMA until it just fitted between the OSL and the scalar floor, and the most distal portion of the nerve was reached by maximizing the angle between the vector and the MMA. When this position was reached, we characterized this vector by measuring the rotational and translational components. The rotation of the vector around the MMA was measured on a reconstructed CT slice perpendicular to the MMA by using the posterior RW edge as the 0° starting point (Fig. 1b). We measured the

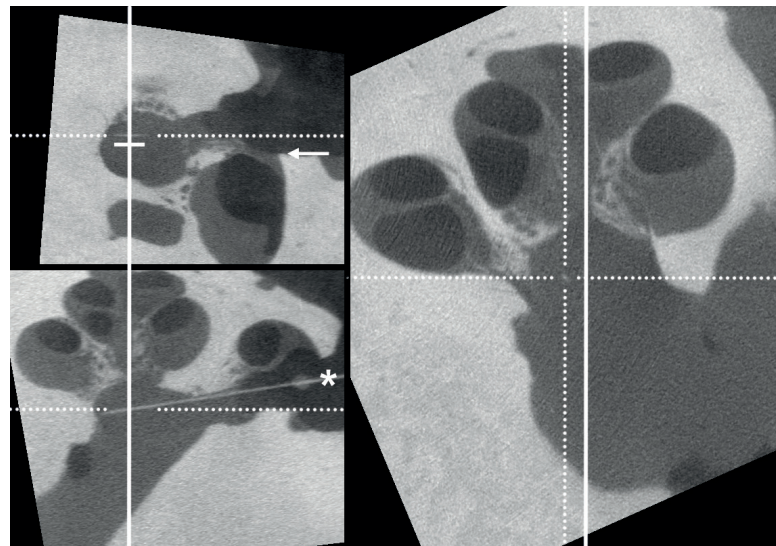


**Figure 1** Positioning and characterization of the vector in the 3D models. (a) Directions of translation (A) and rotation (B and C) of the vector in TB 10; V: vector. (b) Measurement of the angle between the vector and the posterior RW edge in two intersecting orthogonal planes in TB 4. (c) Measurement of the angle between the vector and the MMA (88.4°) and the distance between the vector and the distal nerve end (0.98 mm) in TB 4.



distance between the distal nerve end and the vector on the MMA in a slice in the plane of the axis. The angle between the center of the vector and the MMA could be measured directly (Fig. 1c). We also measured the length of the trajectory from the posterior edge of the facial nerve to the bony wall of the internal auditory canal that the vector reached after it traversed the cochlear nerve. Furthermore, the distance between the CTN and the facial nerve in this plane was measured and we assessed if the vector ran through the CTN. All measurements were repeated three times and the mean values were calculated.

A complete mastoidectomy and posterior tympanotomy was performed on three of the ten TBs. If necessary, the posterior tympanotomy was extended by removing the CTN. The subiculum was drilled away for a full view of the RW, the membrane was removed and, if necessary, the RW was enlarged. Based on the trajectory of the vector, an opening was drilled in the medial wall until the nerve was reached. We used two types of thin-film micro-electrode arrays developed for neural tissue stimulation in animals (NeuroNexus Technologies, Ann Arbor, USA). These 'C-Style' probes (typical thickness 15  $\mu\text{m}$ , shank width 150  $\mu\text{m}$  and total length 14 mm) consist of 16 electrode sites divided over one or four shanks attached to an integrated silicon cable. We used teflon coated Dumont #5 forceps (Fine Science Tools, Heidelberg, Germany) and an otologic pick to insert these



**Figure 2** Multiplanar reconstruction used for postoperative measurements.

Right: mid-modiolar reconstruction, perpendicular to probe. Solid line represents MMA, dotted crosshairs on probe represent other reconstructed planes. Upper left: plane perpendicular to the MMA (solid cross), arrow points at posterior RW edge. Lower left: paramodiolar reconstruction in the plane of the probe, asterisk: probe implanted through the enlarged RW.

probes into the cochlear nerve. After insertion, the proximal part of the probe was glued using Loctite 495 cyanoacrylate adhesive (Henkel, Düsseldorf, Germany) to the anterior margin of the facial nerve for fixation. The implanted TBs were rescanned with the high-resolution protocol to assess probe placement. Using OsiriX 64-bit Imaging Software (Version 3.7) we selected the MMA in a multiplanar reconstruction and used the plane perpendicular to the MMA to measure the angle between the posterior RW edge and the line running parallel to the probe and through the MMA, the distance between the probe and the MMA and the diameter of the nerve in the same direction. In the plane of the probe, parallel to the MMA, we judged the OSL, basilar membrane and insertion depth of the probe and we also measured the angle between the MMA and the probe. In the plane perpendicular to the probe and through the MMA, we measured the distance between the probe and the distal nerve end (Fig. 2).

### 6.3. Results

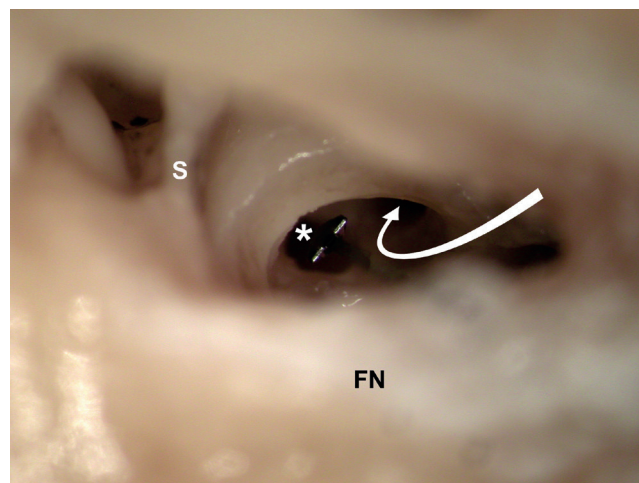
After creating the 3D models, we succeeded in positioning the vectors in every case without violating the predetermined conditions. Table 1 shows the characteristics for each vector. The most important factor for positioning the vectors in the surface models was the distance between the OSL and the ST floor. As the OSL curves around the RW (when seen through the facial recess, the orientation changes from vertical at the superior RW edge to horizontal at the anterior edge<sup>131</sup>), the space between the OSL and the scalar floor increases in the hook region before gradually decreasing further along the cochlear spiral. Positioning the 0.8 mm diameter vector as close to the basal end of the cochlea as possible resulted in a mean angle with the posterior RW edge of 12.8°. This coincided with the vector running through the anteromedial portion of the RW and, in 8 out of 10 cases, just through the adjacent cochlear wall. Therefore, the course of the vector was steeper than the trajectory used in cochlear implantation (i.e. more postero-inferior to antero-superior), which meant that in all cases the vector ran through the inferior portion of the facial recess, close to, or even at the bifurcation of the CTN. The vector intersected the CTN in 7 out of 10 models because either the distance between the two nerves was too small to accommodate the vector or the vector ran oblique with respect to the plane of the facial recess. The vector did not cross the posterior wall of the external auditory canal in any of the models. Inside the internal auditory canal, all vectors ran more or less parallel to the falciform crest and therefore inferior to the facial and the superior vestibular nerves and distal from the point where the inferior vestibular nerve joins the cochlear nerve.

Two probes with one shank and one probe with four shanks were used for implantation in three TBs. Irrespective of the results of the micro-CT analysis, we initially attempted to preserve the CTN in all three TBs. This posed no problem for the opening and enlarging of the RW but prohibited drilling of the planned trajectory in TB1 and TB2,



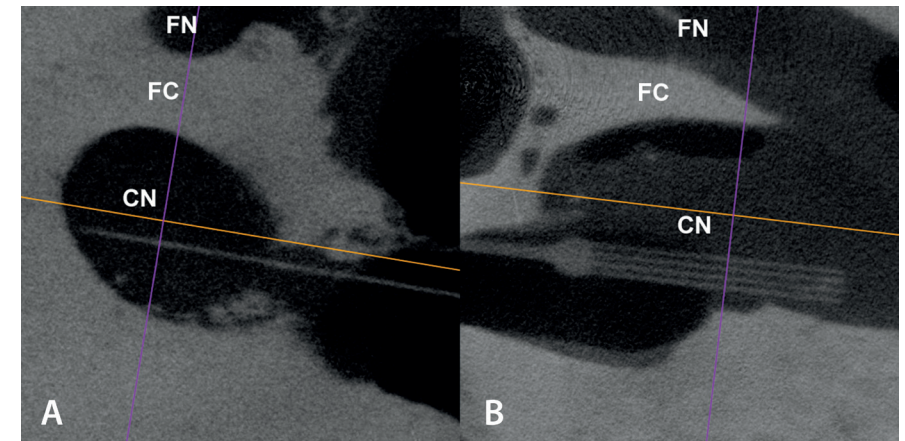
thus confirming the findings in the micro-CT analysis. As drilling the modiolar wall would result in a course just inferior of the internal auditory canal, we decided to extend the posterior tympanotomy by removing the CTN. Although the CTN made it difficult to drill the modiolar wall under the right angle and reduced our view, in TB3 it was possible to access the cochlear nerve while preserving the CTN. Drilling the modiolar wall destroyed some of the nerve fibers running from the organ of Corti to the cochlear nerve. Due to the size of the drill hole, some nervous tissue could be seen, yet there was no view of the nerve as a whole. This made it impossible to determine the axis of the nerve with precision and we therefore had to rely on the vector estimates. All probes were inserted until resistance was felt (Fig. 3).

The post-operative CT scans revealed that the probes were successfully implanted in the cochlear nerve and the OSL and basilar membrane were intact in all three cochleae, however the probe fully traversed the nerve in only TB1 (see Fig. 4a and Video [<http://links.lww.com/MAO/A111>], which demonstrates the implanted probe in a volume rendering of TB1). In TB2 the probe was incompletely inserted (1.9 mm of the 2.9 mm nerve diameter in this direction, although the probe was 6.0 mm in length) and in TB3 the probe was completely inserted but too far in the direction of the nerve rather than perpendicular to it (Fig. 4b). This was expressed by the angle between the probe and the MMA, which was more than 10° smaller than we planned with the vector and also resulted in a larger



**Figure 3** View through the extended facial recess on the probe implanted through the enlarged RW; the probe rests on the facial nerve (FN) and enters a drill hole in the modiolus (asterisk), just below the basilar membrane, at the most basal part of the cochlea; the arrow indicates the course of the basal turn; S: stapes.

distance between the probe and the distal nerve end in both TB2 and TB3 (Table 1). This again, meant that the tip of the probe was proximal to the falciform crest. Also, all three probes crossed inferiorly from the MMA (especially in TB3 where the probe was inserted in the inferior edge of the nerve [distance between probe and MMA was almost half the diameter of the nerve]) (Fig. 4a and b). In TB1 and TB3, this was mainly caused by the probe being directed too inferiorly (the angle between the posterior RW edge and the line running parallel to the probe and through the MMA was too small, with the hole in the modiolar wall at the correct location) and in TB2 the hole in the modiolar wall was too far away from the basal end (the aforementioned angle was too wide, yet the probe still crossed the MMA inferiorly). Furthermore, we found that by drilling the modiolar wall in TB3, the apertures of the inferior cochlear vein and cochlear aqueduct were compromised. In the other two TBs, these structures remained intact.



**Figure 4** Distance between the probe and the MMA in TBs 1 (A) and 3 (B).

Crosshairs represent the position of the MMA, CN: cochlear nerve, FC: falciform crest. Note the probe not fully traversing the nerve in TB 3 due to the non-perpendicular insertion.

**Table 1** Results from 3D models and post-operative scans.

	TB	Side	Angle with RW edge (°)	Distance to lateral nerve end (mm)	Angle with MMA (°)	Vector length (mm)	Distance FN - CTN (mm)	Course through CTN	Distance to MMA (mm)	Nerve diameter (mm)
Pre-op (vector)	1	AD	10.4	1.7	83.8	17.2	0.4	Y		
	2	AS	9.6	1.1	92.6	16.2	0.6	Y		
	3	AS	11.0	1.4	79.5	18.2	2.7	N		
	4	AD	16.7	1.0	88.0	17.3	1.0	Y		
	5	AS	12.4	1.1	85.3	19.9	1.0	Y		
	6	AS	12.0	1.4	85.4	19.2	0.9	Y		
	7	AS	14.8	1.0	84.9	16.3	1.7	N		
	8	AD	16.3	1.4	87.0	18.7	1.5	N		
	9	AD	12.7	1.2	92.9	17.9	0.0*	Y		
	10	AD	12.4	1.5	89.1	17.3	1.0	Y		
Mean										
							1.1			
Post-op (probe)	1	AD	5.7	0.9	84.9			Y	0.3	2.4
	2	AS	13.3	2.1	79.1			Y	0.4	2.4
	3	AS	0.0	2.8	66.7			N	1.1	2.5

\* The vector crosses the facial nerve at the bifurcation of the CTN.

6.4. Discussion

Using 3D surface models based on micro-CT scans of 10 human TBs, we selected the optimal vector for implantation of a cochlear nerve implant via the mastoidectomy posterior tympanotomy approach. Our goal was to find a route through the lateral and medial wall of the ST without compromising the OSL and basilar membrane. We were able to create this vector in every model although it coursed through the CTN in seven cases. Based on these vectors, we implanted a dummy probe in three of the TBs and by using micro-CT we were able to assess the position of the micro-electrode array. Although it was difficult to attain the planned vector position, all probes were successfully implanted into the nerve.

There are few reports on transcochlear approaches for cochlear nerve implantation in humans. Simmons’ report on implanting a four-electrode wire array in two human subjects described how he drilled a hole through the promontory into the scala vestibuli to reach the modiolus and, in doing so, destroyed the nerve fibers in the most basal portion of the first turn <sup>132</sup>. Badi et al. used the extended facial recess approach to access the modiolar nerve in two human TBs. Although this approach sacrifices the CTN, they reported that access to the nerve was 2 x 3 millimeters and that the procedure was not significantly more difficult than the posterior tympanotomy approach used in cochlear implantation. There is no mention of the basilar membrane or OSL, but based on the size of the nerve exposure, these were probably removed <sup>124</sup>.

The transcochlear technique used by Middlebrooks et al. for the implantation in cats consisted of making a hole in the OSL with a 30-gauge needle (0.31 mm outer diameter) <sup>125</sup>. Therefore, the electrode array is inserted in the modiolar trunk of the nerve, while our approach on the other hand, gave access to the complete cochlear nerve, proximal to the lamina cribrosa.

Attempts were made to develop an approach to the modiolar nerve that does not necessitate the opening of the cochlea, but according to Paasche et al., this was not feasible with current technology <sup>133</sup>.

There are several studies on the size of the (extended) facial recess, RW and their topographical relationship <sup>134-137</sup>. Several authors conclude there is no difference in facial recess width between children and adults <sup>134,135</sup>, which means that our results might be applicable to children as well.

One limitation of our study was that all actions in the 3D models were manually performed, which implies certain inaccuracy. To minimize the variation in MMA orientation (which affects placement of the vector and subsequent measurements), we selected the MMA

based on the apical 1.5 turns of the cochlea. Skinner et al. first applied this method because this is the point where the cochlear spiral is coiled the tightest<sup>67</sup>. Nonetheless, as the MMA was separately selected in the pre-operative and post-operative scans, some of the differences between the position of the vector and the probe might be accounted for by a slight variation in orientation of the MMA. Another limitation may be that we based our vector criteria on minimizing damage to labyrinthine structures. In cases where there is a complete loss of labyrinth function, it may be unnecessary to sacrifice the CTN in favor of limiting damage to the labyrinth. Another requirement we set for our vector was that it ran through the most distal portion of the nerve. As a consequence, the vectors ran almost perpendicular to the nerve, yet it is unknown whether this is the best direction for electrical stimulation.

The round window approach itself also has some drawbacks. As the trajectory passes through the modiolar wall of the ST, the spiral ganglion cells in this region are destroyed (a line that runs from the anterior RW edge to the axis of the cochlea, crosses spiral ganglion cells that represent frequencies of about 17 kHz<sup>138</sup>. The loss of these fibers has little clinical relevance as long as the size of the opening in the modiolar wall is limited. Our results demonstrated that drilling the modiolar wall also endangers the cochlear aqueduct and inferior cochlear vein (ICV). While the obliteration of the cochlear aqueduct probably has no effect on the inner ear<sup>139</sup>, damaging the ICV may lead to bleeding into the basal turn. Moreover, extensive or proximal occlusion of this vein in the guinea pig is known to lead to reductions in blood flow, changes in cell structure and cochlear function (in contrast to more distal occlusion, which has less severe effects)<sup>140, 141, 142</sup>. However, the collateral drainage system in man is probably more effective, via the vein of the cochlear aqueduct (which may be absent or very small in the guinea pig)<sup>143</sup>. Contrary to the principles of soft surgery in cochlear implantation, the cochlea is opened for a longer period, drilling of the modiolar wall releases bone dust inside the cochlea and suctioning of perilymph might be necessary for visualization. These factors will most likely lead to loss of residual labyrinthine function<sup>144,145,146</sup>.

Also, a posteriorly angled external auditory canal might possibly impede visualization of the RW membrane. However, we did not encounter this problem in our models or in the temporal bones, probably because of the inferior to superior direction of our vector (in contrast to a more posterior to anterior direction in conventional cochlear implantation) and removal of the CTN.

One of the dangers of intraneural implantation is causing damage to the fibers of the cochlear nerve. Although most probes slid quite easily between the nerve fibers in our study, we noticed that it was harder to insert probes with broader shanks. Packing of the RW to stop perilymph leakage after implantation should also be done with great care in order to prevent electrode movement and nerve damage. Histological results of chronic

implantation and stimulation in both animal and human subjects, ranged from little damage to nerve fibers<sup>122, 147</sup> to extensive loss of spiral ganglion cells and axons, probably due to difficult electrode insertion and chronic implant movement<sup>148</sup>. A pneumatic insertion device has been developed to minimize tissue damage<sup>149</sup>, but more research on this subject is essential.

Another drawback is that while intraneural implantation gives access to the entire cochlear frequency spectrum, the tonotopic organization of the cochlear nerve is much more complex than that within the cochlea. Therefore, postoperative mapping will be more challenging than with conventional cochlear implants (probably similar as in auditory brainstem implantation).

Unlike the guinea pig's cochlea, which protrudes in an air-filled bulla, the human cochlea is embedded in bone, which makes it hard to choose the right trajectory in the modiolar wall to reach the desired part of the cochlear nerve. As the optimal vector runs through- or slightly superior- from where the CTN branches from the facial nerve and through the anterior part of the RW, these landmarks should be used to guide drilling of the modiolar wall. With regard to the anteroposterior orientation, we recommend starting the trajectory as close as possible to the anterolateral surface of the facial nerve (in the facial recess) and pass as close as possible to the medial side of the bony spiral lamina to insert the probe almost perpendicular to the cochlear nerve and close to the fundus of the cochlea at the level where the nerve is still separated from the facial and vestibular nerves.

We also recommend removing the CTN if the round window approach is used for intraneural implantation. Based on our CT findings, in 3 out of 10 TBs it was possible to drill a trajectory that was 0.8 mm in diameter without sacrificing the CTN. An important aspect to consider when drilling the modiolar wall is the risk of the drill bur becoming lodged in the inferior portion of the facial recess as the bur shaft may be wider than the head of the bur. This may lead to heat damage to the facial nerve. Also, removing the CTN gives a better view on the exposed nerve and makes it easier to enlarge the drill hole in the modiolar wall in an anterior direction to expose a larger part of the nerve for implantation of a larger electrode array, if desired. This is supported by the results in TB3 where the CTN was preserved but the implantation was more difficult, the cochlear aqueduct and ICV were damaged and the results were less preferable than in the other cases.

Sectioning the CTN has three disadvantages: it can lead to loss or alteration of taste, decrease in tongue sensation or, less common, xerostomia. Although these symptoms occur in 40-60% of patients, for 94-96% of these patients the symptoms are no longer present two years post-surgery. Electrogustometry thresholds on the other hand, often remain elevated<sup>83,84</sup>. A possible solution to spare both the CTN and the OSL would be to pass inferiorly from the CTN. This however, would require drilling a large cochleostomy

instead of enlarging the round window and as such, sacrificing lower frequency spiral ganglion cells and inserting the probe less perpendicular into the nerve (as the descending portion of the facial nerve runs somewhat anteriorly).

Intraneural implantation could be an alternative for patients with a severely ossified or an obliterated cochlea. Based on current treatment, these patients are required to undergo either a drill-out of the ST or auditory brainstem implantation. Both these procedures lead to less favorable results than 'regular' cochlear implantation<sup>150,151</sup>. Alternatively, intraneural stimulation may be used as a supplement to current cochlear implant systems; the intraneural implant could stimulate low frequency fibers while the cochlear implant stimulates the remaining frequencies.

## 6.5. Conclusion

Based on 3D models of 10 TBs and applied surgically in 3 TBs, we attempted to create a transcochlear surgical approach to implant a cochlear nerve prosthesis that preserves both the OSL and basilar membrane and sacrifices only the most basal spiral ganglion cells. Although our conclusions are based on a relatively small series of TBs, we believe that the optimal trajectory runs from the point where the CTN branches from the facial nerve, through the anterior RW edge and modiolar wall, to the most distal portion of the cochlear nerve. Both our CT and clinical findings suggest that the CTN should be sacrificed to perform this procedure.

## IV | Surgical planning and evaluation of cochlear nerve implantation

### 7. The extended infralabyrinthine approach

#### Submitted as:

The extended infralabyrinthine approach for cochlear nerve implantation with  
a penetrating electrode array in the human temporal bone

Theunisse HJ, Gotthardt M, Mylanus EA.



## Abstract

An electrode array implanted directly into the cochlear nerve might overcome limitations imposed by current cochlear implant systems. To demonstrate the feasibility of extra-cochlear cochlear nerve implantation, we used an extended infralabyrinthine approach (EILA) to allow access to the nerve. After obtaining pre-operative micro-CT scans for morphometric evaluation, the EILA was attempted in ten human formalin-fixed temporal bones. If access to the nerve was gained, a dummy probe was implanted and a post-operative micro-CT scan was made for evaluation. This was successful in 8 out of 10 temporal bones. In the remaining 2, a high jugular bulb blocked access to the nerve. Assessment of the implantations revealed that all probes were implanted into the cochlear nerve, 1 traversed into the facial nerve and in 2 cases, the basal turn was damaged. Success of the approach was related to the distance between the jugular bulb and the posterior semicircular canal. The EILA is a complex procedure, which allows transmastoid, extra-cochlear access to the cochlear nerve for implantation of an auditory prosthesis. Patients with high jugular bulb should be excluded by pre-operative CT analysis.

## 7.1. Introduction

Parallel to the ongoing success of cochlear implantation, several studies have been published in the last decade on the subject of intraneural cochlear nerve stimulation<sup>152,153</sup>. There are several reasons to consider a cochlear nerve implant as an alternative auditory prosthesis. One reason is that the progress in performance with cochlear implants (CIs) seems to have slowed down in recent years. Since their introduction, CIs have exceeded all expectations and new applications such as bilateral implantation and electro-acoustic stimulation have produced significant improvements, but representation of temporal fine structure (which is necessary for speech perception in noise and music appreciation) is still limited<sup>28,154</sup>. Optimizing electrode placement and current steering seems promising, but has led to little improvement in speech perception so far<sup>70,72,155,156</sup>. Although it is difficult to evaluate such effects due to the heterogeneity of results in CI recipients, some of the limits inherent to intrascalar stimulation may not be overcome. Intraneural implants may offer the prospect of higher spatial resolution, lower stimulation thresholds and stimulation of low-frequency fibers, thus overcoming these limits<sup>148</sup>. Another reason is the possible application of an intraneural implant in patients with compromised cochleae. Both cochlear implantation after cochlear drill-out in patients with non-patent cochleae and auditory brainstem implantation, lead to speech perception outcomes that are less favorable than with regular cochlear implantation<sup>150,151</sup>. A third possible application might be to use it as a supplement to current CI systems: the low frequencies that are difficult to stimulate with CIs, can be stimulated with penetrating electrodes, while the other frequencies are stimulated with the CI.

While animal studies with cochlear nerve implants have shown some promising results, implementation in humans is still far away. One of the steps towards tests in human subjects is the development of a surgical approach for intraneural implantation.

In animal studies, and also in three human subjects in the 1960's and 70's, a transcochlear approach was used to implant electrodes in the modiolar portion of the nerve<sup>119,124,132</sup>. We have studied a transcochlear approach to the most distal portion of the nerve ourselves, but this approach required prolonged opening and drilling on the inside of the cochlea (most likely leading to loss of residual labyrinthine function), gave limited access to the nerve and required sacrificing the chorda tympani nerve, at least when the vestibulum and osseous spiral lamina were to be spared<sup>157</sup>.

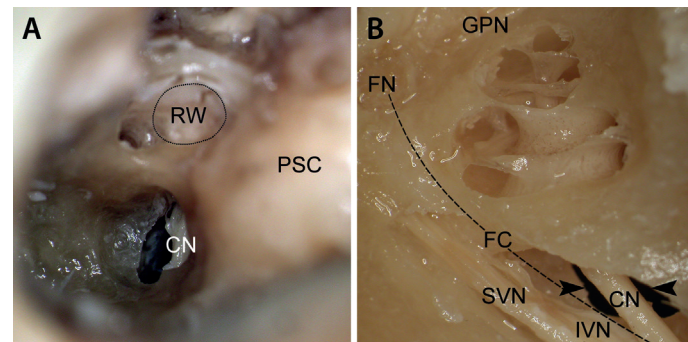
The infralabyrinthine approach was introduced by Vernick to gain extracranial access to at least the proximal half of the internal auditory canal (IAC) while preserving the bony labyrinth, which allowed selective sectioning of the vestibular nerves in patients with severe vertigo<sup>158</sup>. We explored the possibility to gain access to the antero-inferior quadrant and most distal portion of the cochlear nerve (where the cochlear nerve is completely separated from the facial and vestibular nerves and least subject to movement of the



brain) with a modified version of this approach, by partially removing the mastoid tip and drilling towards the IAC from an inferior to superior direction (Fig. 1). The goal of this study was to investigate the feasibility of implanting a penetrating auditory prosthesis in the cochlear nerve using this extended infralabyrinthine approach (EILA) in the human cadaver temporal bone (TB) specimens.

## 7.2. Material and methods

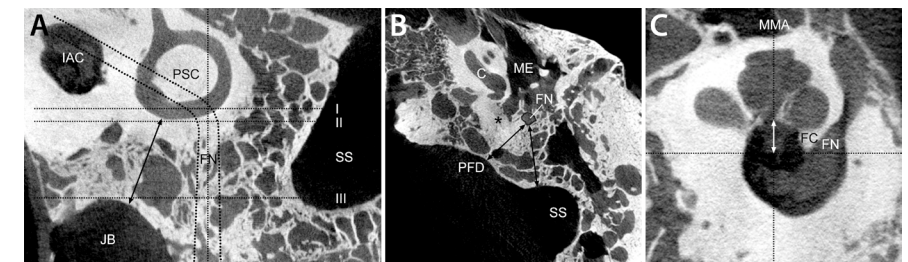
Ten randomly selected, formalin-fixed human TBs (6 left and 4 right) were cut to a cylindrical shape of 4 x 6 cm to fit the maximum field of view of the micro-CT device of an Inveon™ small-animal PET/CT system (Siemens Healthcare, Erlangen, Germany), while preserving all anatomical landmarks that can limit the surgical approach. The following acquisition protocol was used: X-ray source: 80 kV, 500 mA; exposition time: 1000 ms; rotation: 202°, 202 steps; FOV: 60.8 x 40.6 mm. We exported the reconstructed image files with a voxel size of 0.04 mm to DICOM format with Inveon Research Workplace and conducted distance measurements using OsiriX MD (Pixmeo, Geneva, Switzerland).



**Figure 1** Exploratory attempts to access the cochlear nerve (CN) using the extended infralabyrinthine approach in a human temporal bone (left side). **A:** Transmastoid surgical access to the CN in the opened internal auditory canal, just proximal to the cochlea. The opened and enlarged round window (RW) provides a view on the scala tympani and osseous spiral lamina; dotted line indicates the original RW position. Facial nerve removed for photograph. **B:** View from the middle fossa on cochlea and internal auditory canal in the same temporal bone. Horizontal segment of FN, geniculate ganglion and greater petrosal nerve (GPN) removed, and cochlea and internal auditory canal opened for illustrative purposes. Arrowheads indicate the transmastoid access to the CN, dashed line indicates original course of the FN. FC: falciform crest; SVN and IVN: superior and inferior vestibular nerves.

In a multiplanar reconstruction we selected the plane of the posterior semicircular canal (PSC; Fig. 2A). Because the PSC is not completely 'flat', we used the plane with the widest canal diameter. In this plane, we measured the distance between the PSC and the jugular bulb (JB). When the JB was located medially from this plane, we measured the distance to the inferior margin of the skull base. By scrolling laterally to the level of the facial nerve (FN), we set one line of the crosshairs over the axis of the mastoid segment of the FN so that we were able to move the plane perpendicular to this axis to different levels along the FN to conduct our measurements. Level I was at the point where the FN crossed the midpoint of PSC; in this plane we measured the distance between the FN and the PSC (in most cases this was the ampulla of the PSC). Level II was just inferior to the PSC (Fig. 2B); here we measured the distance between the FN and the posterior fossa dura (PFD)/endolymphatic sac and the distance between the FN and the sigmoid sinus (SS; in cases with a less protruding sinus, this was the point of transition between the sinus and the PFD). Level III was at the most superior aspect of the JB, where we measured the distance between the FN and the top of the JB. Next, we selected the mid-modiolar axis (MMA) based on the apical 1.5 turns of the cochlea. In a mid-modiolar reconstruction, we measured the distance from the most distal part of the IAC to the proximal edge of the falciform crest (Fig. 2C) and to the distal edge of the singular foramen (transmitting the posterior ampullar nerve) along this axis.

After acquiring the micro-CT images, a complete mastoidectomy and posterior tympanotomy was performed on each TB. Care was taken to completely skeletonize the

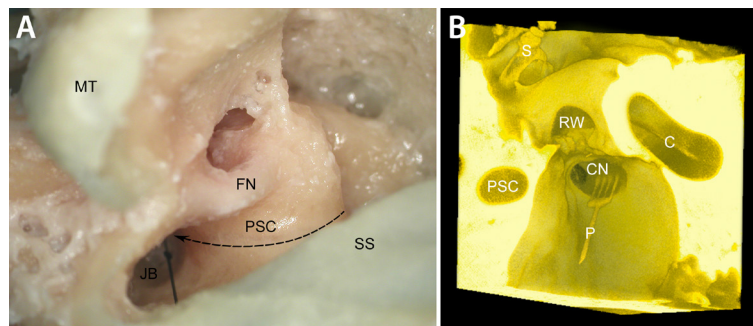


**Figure 2** **A:** Plane of the posterior semicircular canal (PSC) with a projection of the course of the facial nerve (FN; curved dotted lines) and its axis (vertical dotted line) in TB 9. The distance PSC to jugular bulb (JB) was measured in this plane (double arrow). Horizontal dotted lines I to III designate the levels of the planes used for the other measurements. IAC: internal auditory canal; SS: sigmoid sinus. **B:** Example of the measurements at level II in TB 5. Arrows indicate the shortest distances FN (outlined in black) to posterior fossa dura (PFD) and FN to SS. ME: middle ear; C: cochlea; \*: inferior edge of PSC. **C:** Example of the measurement of the length of the falciform crest (FC), from its proximal edge to the distal nerve end along the mid-modiolar axis (MMA), in a mid-modiolar reconstruction of TB 9.



SS, the PFD and endolymphatic sac and the mastoid segment of the FN. Through the facial recess, bone was removed anterior and medial to the FN. Next, the PSC was blue-lined in the direction of the ampulla and the retrofacial cells were removed, exposing the JB. Following the retrofacial tract, drilling was continued just proximal from the round window, towards the IAC (Fig. 3). By drilling in this direction, both the cochlear aqueduct (CA) and the inferior cochlear vein (ICV) were encountered and sacrificed. In order to visualize the most distal part of the IAC it was necessary to extend the mastoidectomy inferiorly by drilling away part of the mastoid tip and lowering the edge of the mastoidectomy to the level of the SS. However, the bone covering the SS was preserved in all TBs. Bone was removed from the antero-inferior portion of the IAC and the exposed dura was slit along the axis of the canal, uncovering the cochlear nerve underneath.

For the implantation we used several types of thin film microelectrode arrays, developed for stimulation of neural tissues in animals (NeuroNexus Technologies, Ann Arbor, USA; Fig. 4). Using Teflon coated Dumont #5 forceps (Fine Science Tools, Heidelberg, Germany), we inserted these probes into the most distal portion of the cochlear nerve. By aiming slightly laterally, we attempted to let the tip of the probe rest on the falciform crest after penetrating the cochlear nerve, preventing insertion into the FN. After the insertion, the proximal part of the probe was glued to the bone covering the PFD using Loctite 495 cyanoacrylate adhesive (Henkel, Düsseldorf, Germany) to prevent displacement.

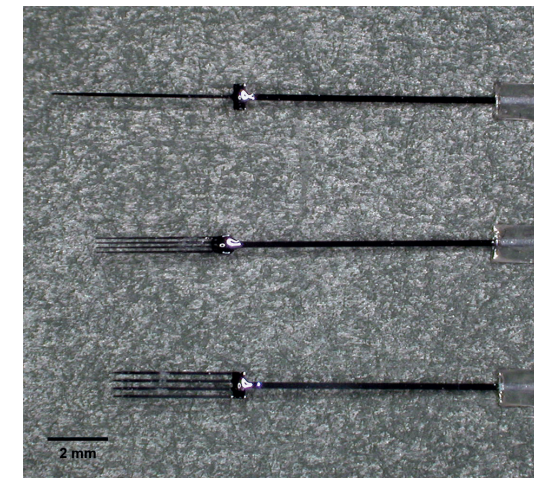


**Figure 3** **A:** A single-shank probe implanted through the extended infralabyrinthine approach in TB 4. Inferior view on the TB after partial removal of the mastoid tip (MT). Dashed arrow follows the blue-lined posterior semicircular canal (PSC) and points towards the internal auditory canal. JB: jugular bulb; FN: facial nerve; SS: sigmoid sinus. **B:** Volume rendering of a 4-shank probe (P) implanted in the cochlear nerve (CN) in TB 9. Some debris from the accidental fenestration of the medial side of the cochlea is visible through the round window (RW). Cross-section through the basal turn (C) permits a view on the osseous spiral lamina. S: stapes.

After implantation, another micro-CT scan was obtained from each TB to assess the position of the probe. In order to maximize the soft tissue contrast and visualize the probe, we used the following acquisition protocol: X-ray source: 60 kV, 500 mA; exposition time: 9000 ms; rotation: 360°, 720 steps; FOV: 31.8 x 21.2 mm. The reconstructed voxel size of these images was 0.01 mm.

In a multiplanar reconstruction we evaluated the implantation by obtaining the following parameters: in the plane perpendicular to the probe and through the MMA, we measured the distance between the probe and the MMA, the nerve diameter in this direction, the distance between the probe and the distal nerve end along the MMA and determined whether the probe ran antero-inferior or posterosuperior to the MMA. In the plane of the probe and parallel to the MMA, we measured the angle with the MMA, the insertion depth and the nerve diameter in this direction. To ascertain that the narrow tip of the probe was completely visualized, we checked the length of the shank in the micro-CT scan with the manufacturer's specifications. We also evaluated if one of the following structures was damaged: PSC, posterior ampullar nerve, basal turn, ICV and CA.

Using SPSS 16.0 (SPSS Inc., Chicago, USA), we tested for relationships between the anatomic measurements in the pre-operative micro-CT scans, success of the approach, the probe characteristics, and results of the implantation.



**Figure 4** The various probe designs used in this study. These probes consist of 16 electrode sites divided over one or four shanks attached to an integrated silicon cable, with a typical thickness of 15 µm, shank width of 150 µm and total length of 14 mm ('C' style probes). The probes consist of the actual probe (the tip), a silastic bead coated on a tab for handling, and a more flexible integrated ribbon cable.

### 7.3. Results

The results from the pre-operative distance measurements and related descriptive statistics are displayed in table 1. We found the largest variation in the distance PSC to JB, which had a coefficient of variation (CV) of 0.46, followed by the distance FN to JB with a CV of 0.19. In the plane parallel to the PSC (Fig. 2A), the JB was located anterior to the FN in all cases. In 3 TBs, the JB was located medially to this plane and thus the distance from the PSC to the inferior edge of the skull base was measured instead of to the JB. We did not find significantly different distances between right and left TBs.

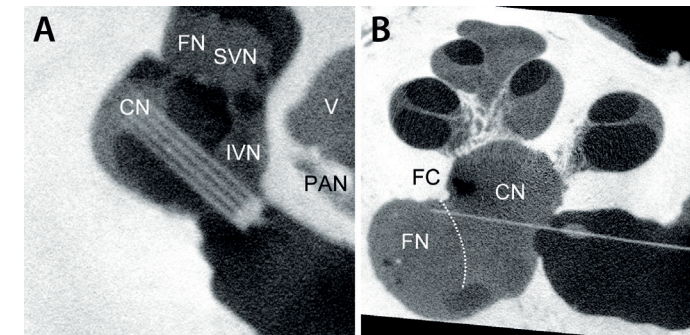
Using the EILA, we succeeded in opening the IAC in 8 out of 10 TBs, while no further problems were encountered during the procedure. In TB 3 and TB 10, the approach was blocked because the distance between the PSC and the JB was too small to allow drilling towards the IAC. We did not attempt to depress the JB in these cases and sectioning the endolymphatic duct (which was suggested by Vernick in case of a high JB) was not useful because our approach was inferior to the duct. The SS did not prove to be an obstacle for the approach in any of the TBs.

After opening the IAC in TB 1, we found that the cochlear nerve had accidentally been removed, probably during removal of the TB from the cadaver. In the remaining 7 TBs, opening the IAC allowed wide exposure of the nerves and the probes could be inserted at the preferred location and angle (Fig. 3). Eventually, we implanted 3 wide and 2 narrow 4-shank probes (total width of 0.87 and 0.55 mm, respectively) and 2 single-shank probes of different width and length. We noticed that the narrow 4-shank probes were easier to implant than the wide ones, probably because the shanks themselves were also narrower. Nonetheless, all probes could be inserted without force or visible damage to the nerve.

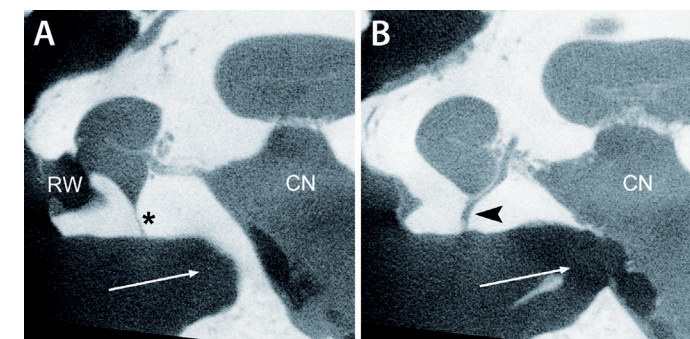
Post-operative micro-CT scans confirmed that all probes were implanted in the cochlear nerve, although it was sometimes difficult to confirm that the probe did not enter the inferior vestibular nerve (called the saccular nerve at this point), based on these images (Fig. 5a). All probes were implanted distal to the point where the singular canal meets the IAC, so it was impossible that they entered the posterior ampullar nerve. Even though we inserted the probes until resistance was felt, some of the probes did not fully traverse the cochlear nerve. In TB 6, on the other hand, the tip of the probe entered the FN after it crossed the cochlear nerve (Fig. 5B), which may be attributed to the fact that the angle with the MMA was the smallest, and the distance to the distal nerve end was the largest of the implanted TBs in the series. Also, this was one of the two TBs where the probe ran posterosuperior to the MMA and was directed too much cranially. Four out of 7 probes ran medially to the falciform crest at the level of the MMA.

In all the TBs where the EILA was successful, we found that the ICV and CA were indeed both destroyed (Fig. 6). Furthermore, we detected that we accidentally created a fenestration in the basal turn of the cochlea in 2 TBs (Fig. 3B). In none of the TBs, the PSC or the posterior ampullar nerve was damaged.

Specific measurements on the implanted probes are displayed in Table 1.



**Figure 5** **A:** Micro-CT image of a 4-shank probe implanted in the cochlear nerve (CN) in TB 7. The inferior vestibular nerve (IVN) runs adjacent to the probe, but accidental insertion into this nerve cannot be ruled out with absolute certainty based on this image. Note the posterior ampullar nerve (PAN) next to the drill-hole. FN: facial nerve; SVN: superior vestibular nerve; V: vestibulum. **B:** Tip of the 4-shank probe inserted into the facial nerve (FN) after fully traversing the CN in TB6. The probe runs proximal to the falciform crest (FC).



**Figure 6** **A:** Destruction of the cochlear aqueduct (\*) in TB 4. White arrow indicates direction of the approach. RW: round window; CN: cochlear nerve. **B:** Destruction of the inferior cochlear vein (arrowhead) in TB 4. Part of the implanted probe is visible below the white arrow.

**Table 1** Results from pre-and postoperative measurements in the micro-CT scans.

TB	PSC-JB (mm)	FN-PSC (mm)	FN-PFD (mm)	FN-SS (mm)	FN-JB (mm)	DNE-FC (mm)	DNE-SF (mm)	Probe- MMA (mm)	CN Ø 1 (mm)	Probe- DNE (mm)	∠ Probe- MMA (°)	Insertion dept (mm)	CN Ø 2 (mm)
1	8,91	4,11	6,38	12,97	10,59	2,38	4,78						
2	11,15 <sup>†</sup>	3,27	7,09	13,40	11,57	1,82	3,36	0,28	2,50	1,05	116,48	1,44	1,44
3	1,49	2,93	6,85	12,77	10,48	1,58	3,86						
4	11,70	4,04	6,91	14,34	16,03	2,25	5,68	0,84	3,12	2,34	110,18	1,33	2,21
5*	10,84 <sup>†</sup>	3,73	8,71	11,93	14,13	1,80	4,73	0,04	3,99	2,01	105,15	0,51	1,08
6	11,73 <sup>†</sup>	3,37	7,27	11,21	13,68	1,88	3,55	0,40	3,90	2,40	99,51	3,65 <sup>†</sup>	3,38
7	6,51	3,25	8,96	13,67	11,20	1,37	3,84	0,14	3,22	1,46	100,43	1,44	1,66
8	11,26	3,88	8,15	11,68	15,48	1,83	4,75	0,08	1,29	0,26	120,59	1,83	1,83
9*	7,85	3,58	7,05	9,59	12,82	1,57	3,76	0,25	1,87	1,25	113,44	2,78	3,16
10	2,36	3,86	6,89	12,69	8,64	2,25	5,14						
Mean	8,38	3,60	7,42	12,42	12,46	1,87	4,34	0,29	2,84	1,54	109,40	1,85	2,11
SD	3,83	0,39	0,87	1,37	2,37	0,33	0,77	0,27	1,01	0,77	8,05	1,04	0,86

TB 1 was not implanted due to an absent CN and TB 3 and 10 were not implanted due to a high JB. DNE: distal nerve end; SF: singular foramen; CN Ø 1: nerve diameter in the line of the probe to MMA measurement; CN Ø 2: nerve diameter in the line of the insertion depth measurement. \*: basal turn of the cochlea was accidentally fenestrated in these TBs; <sup>†</sup>: because JB was located medially to the plane of the PSC, the distance to the inferior edge of the skull base was measured instead; <sup>†</sup>: insertion depth exceeds nerve diameter due to crossing over into the FN.

Both the distances PSC to JB and FN to JB in the TBs where the approach was unsuccessful ( $\bar{x}$  = 1.92 and 9.56 mm, respectively), differed significantly from the TBs in which the approach was successful ( $\bar{x}$  = 10.99 and 13.25 mm, respectively),  $W_s = 3.00$ ,  $z = -2.09$ ,  $p = .04$ ,  $r = -.66$  for both (Wilcoxon rank-sum test). Parametric tests (disregarding the small sample size) suggests that the success of the approach might have a stronger correlation with the distance PSC to JB,  $r_{pb} = .89$ ,  $p$  (one-tailed)  $< .01$ , than with the distance FN to JB,  $r_{pb} = .78$ ,  $p$  (one-tailed) = .02 (Point-biserial correlations). The distances PSC to JB and FN to JB were also significantly correlated,  $r_s = .82$ ,  $p$  (one-tailed)  $< .01$  (Spearman's rho).

The minimum distance between the PSC and the JB in the TBs where the approach was successful was 6.5 mm. The maximum distance in the TBs where the approach was unsuccessful was 2.4 mm. This means that the minimum distance that is required for this approach to be possible, probably lies somewhere between these 2 values, but our series was too small to provide a more accurate value.

There was a significant negative relationship between the width of the shank(s) of the probe and percentage implantation depth (implantation depth / nerve diameter in the direction of implantation \* 100%),  $\tau = -.74$ ,  $p$  (one-tailed) = .02 (Kendall's tau).

There was no correlation between the length of the falciform crest and the probe crossing over into the FN.

## 7.4. Discussion

There are only 2 reports on the infralabyrinthine approach from the perspective of cochlear nerve implantation that we are aware of. Middlebrooks et al. reported that a group of surgeons at the University of Michigan have explored the ILA to provide access to a peripheral portion of the nerve, but found that access was blocked by the JB in about one-third of the TBs <sup>153</sup>. Paasche et al. used a surgical navigation system to find possible trajectories to the cochlear nerve without damaging the labyrinth in 5 human TBs. They attempted an approach in dorsomedial direction that is somewhat similar to the EILA and concluded that it provided the best access to the nerve, but that it was technically not feasible <sup>133</sup>.

Most of the other literature on the infralabyrinthine approach to the IAC focuses on the possibilities to use this approach for vestibular nerve sectioning.

Including Vernick, a total of 13 patients that underwent vestibular nerve section using the ILA were reported in 3 studies. No intraoperative problems were encountered and hearing preservation was achieved in 10 patients. Technical difficulties were caused by anatomic variations such as a high JB or an anteriorly oriented SS, but the authors report that these obstacles can be easily overcome by carrying out the dissection at a higher level after cutting the endolymphatic duct or by depressing the sigmoid sinus and/or



posterior fossa dura, respectively. Tomoda et al. also propose that a CT scan should be made prior to surgery<sup>158-160</sup>. Because we had to pass in between the PSC and the JB, cutting the endolymphatic duct was not helpful in case of a high JB. We did not encounter problems from an anteriorly placed SS, probably because we passed in between the JB and the vertical segment of the SS after partial removal of the mastoid tip.

Several temporal bone studies focused on the relevant surgical anatomy for both this approach and for access to the sinus tympani and the hypotympanum through the retrofacial air tract for the removal of pathologic lesions (such as glomus tumor or cholesteatoma). Because distance measurements were done either directly in the dissected temporal bones or in standard CT reconstruction planes, results cannot directly be compared to ours. Nevertheless, most authors confirmed our findings that JB position and anatomy are highly variable while the position of the FN and PSC, as well as the distance FN to PFD are relatively constant (except for Maniglia et al., who found a wide variation in all their distance measurements with a CV ~ 0.35)<sup>161-164</sup>.

The distances JB to PSC and JB to FN were considered critical in gaining access to the IAC. A high jugular bulb limited or blocked access to the IAC or sinus tympani in most cases and was reported in 6-20% of pediatric and 8-63% of adult temporal bones<sup>164-167</sup>.

There are a number of aspects of the surgical procedure itself that have to be taken into consideration before this approach can be applied clinically. First, there is very little known about the effects and results of intraneural cochlear nerve stimulation in man. Histologic results of chronic implantation and stimulation in both animal and human subjects, ranged from little damage to nerve fibers<sup>122,147</sup> to extensive loss of spiral ganglion cells and axons, probably because of difficult electrode insertion and chronic implant movement<sup>148</sup>. Currently, there is no commercially available intraneural auditory prosthesis and it is unknown how a modern intraneural implant will compare to a CI or an ABI in human subjects. If implemented, new speech processing strategies will need to be developed and postoperative mapping will probably be more challenging than with conventional CIs.

Second, in our study we used TBs that had all soft tissues removed and therefore we disregarded some of the steps that would be necessary in a real-life surgery. Because we lowered the posterior edge of the mastoid tip to the level of the SS, this would require sectioning the posterior part of the attachment of the sternocleidomastoid and digastric muscle on the mastoid tip. The procedure (which is considered standard in a canal wall down technique by some surgeons<sup>168</sup>) has elsewhere been described as part of the infratemporal fossa approach without mobilization of the FN<sup>169,170</sup>. We would therefore suggest to place the patient in a lateral position with the head rotated horizontally to minimize torsion to the contralateral jugular vein, as recommended by Miller et al. for all posterior petrosectomy procedures<sup>171</sup>. In combination with a postauricular incision that is

extended into the neck, this would provide a posteroinferior access to the IAC that is optimal for cochlear nerve implantation. Whole cadaver surgery could be used to investigate this.

Third, by drilling just medially from the round window niche towards the IAC, both the CA and the ICV are sacrificed. The CA extends from the basal turn of the cochlea towards the posterior cranial fossa and is thought to play a role in perilymphatic pressure regulation, but its exact role in inner ear physiology is not well understood. In a series of 101 disease-free TBs, Gopen et al. found a patent aqueduct in 34 cases, an aqueduct filled with loose connective tissue in 60 cases and an aqueduct occluded by bone or fully obliterated in 7 cases<sup>172</sup>. These findings, combined with reports on experimental occlusion of the CA in cats<sup>173</sup> and guinea pigs<sup>139</sup>, where no influence on cochlear function and morphology was found, support the theory that obliteration of the aqueduct has no harmful effects on inner ear function.

The ICV runs parallel to the CA and transfers the major portion of the venous blood from the cochlea, the utricle and the saccule to the dural sinus. The vein of the vestibular aqueduct, which drains in the SS, transfers venous blood from the three ampullae and semicircular canals. Collateral vessels exist between these two systems, but it is not well known if the vein of the vestibular aqueduct is able to process the complete venous drainage of the labyrinth when the ICV is occluded. Experiments in guinea pigs have shown that occlusion of the distal portion of the ICV leads to dilatation of some of the proximal vessels without significant changes on histological examination<sup>142,174</sup>, while a more extensive occlusion of the vein can lead to reduction in blood flow, changes in cell structure and cochlear and vestibular function<sup>140,175,176</sup>. However, the vein of the CA in guinea pigs is very small or might even be non-existent<sup>143</sup>, so therefore these results are probably not directly applicable to man. Nonetheless, more knowledge on the venous drainage of the human labyrinth is necessary before this approach can be applied in patients with residual labyrinthine function.

Fourth, the EILA remains a complex procedure that risks damaging the FN, PSC, JB, posterior ampullar nerve and basal turn of the cochlea. Although the retrofacial air tract is known to be well-developed<sup>177</sup>, its size is determined by the location of the JB and the SS. In our study, we did not encounter problems from an anteriorly positioned SS, but the distance between the PSC and the JB clearly determined if the approach was possible or not. We estimate the minimum distance PSC to JB that is necessary for the approach to succeed, to be about 3.0 mm, but a larger series is needed to determine this more precisely. The reported incidence of high JB varies highly according to the definition that is used, but based on our experience and the papers that list individual cases, we would estimate the incidence of a JB to PSC distance smaller than 3.0 mm to be about 10-35%<sup>163,164</sup>. Therefore, we would recommend to obtain a pre-operative CT scan and measure the distance PSC to JB, preferably in a multiplanar reconstruction, to assess whether the

EILA is blocked by a high JB or not. Various authors describe the technique for lowering a high JB for translabyrinthine surgery by skeletonizing the JB and pushing it downwards while applying bone wax and oxidised cellulose<sup>178,179</sup>. Although this technique may even be applied with an intact labyrinth, it is argued that manipulation of the delicate bulb can lead to troublesome bleeding and compression may even cause neural injury<sup>180</sup>. Taking all these points into consideration, the EILA should only be performed by an experienced otologic or skull base surgeon.

## 7.5. Conclusion

With this study, we demonstrated the feasibility of using the EILA for the implantation of an intraneural auditory prosthesis in the human TB. The EILA has the advantage that it gives access to the most distal portion of the cochlear nerve with late opening of the dural space and sparing of the bony labyrinth. Contrary to the transcochlear approach, it gives a complete view on the cochlear nerve, allowing a more controlled implantation. The disadvantage is that it is a complex surgical procedure that can be complicated by a high JB. Pre-operative CT scanning is necessary to see whether access to the IAC is possible without lowering the JB. The distance between the PSC and the JB can serve as a good indicator for this. Implanting a probe using this approach brings the risk of the probe entering the FN after crossing the CN. This can be prevented by opening the IAC close to the fundus of the cochlea, implanting in the most distal portion of the nerve (at the level of the falcicorm crest) and aiming both laterally (thus creating a more than 90° angle with the MMA) and anteriorly. This means that the direction of implantation is different from the trajectory of the approach. Furthermore, more research is necessary on the effects of sacrificing the ICV, if this approach is to be applied in patients with residual labyrinthine function. Based on these results, we conclude that the EILA is a suitable approach for the implantation of an intraneural auditory prosthesis, when this is to be attempted in human subjects.

## V | Closing

### 8. General discussion



Cochlear implantation has become standard care for restoring hearing in patients with congenital or acquired severe to profound bilateral hearing loss. Although results have far surpassed initial expectations, limitations such as reduced speech perception in noise and poor music appreciation remain. Most of these limitations are inherent to the implant design. Furthermore, complications rates remain relatively high compared to other fields of otologic surgery. This thesis explores several fields for improvement: low-dose computed tomography for postoperative imaging of the implant (to evaluate [new] electrode designs), medical complications and device failures in a large clinical series (to identify risk factors and reduce complications) and surgical approaches for cochlear nerve implantation (to investigate direct electrical nerve stimulation as an alternative for cochlear implantation). This chapter discusses the most important methodological considerations, provides a brief summary of the main findings and their implications on clinical practice, and directions for future research.

## 8.1. Methodological considerations

Two study designs were used in this thesis: human cadaver temporal bones studies and a retrospective chart review/observational study. Cadaveric studies allow safe investigation of (potentially) hazardous interventions (such as repeated radiation exposure and testing new surgical techniques), but their external validity always needs to be considered. The biggest issues concern the difference between a whole body or a sole temporal bone, and handling live or, in this case, formalin-fixed tissue. In the imaging study, this was largely overcome by using a human skull phantom. The implanted otic capsule was embedded in a plastic ring with formalin and gelatin to mimic radiation absorption similar to a human head. Nevertheless, this still remains a substitute for clinical conditions and real-life issues like motion artifacts are not taken into account. The same applies for the studies on cochlear nerve implantation: while surgical planning and execution may be feasible in temporal bones, that does not mean that the same procedure is straightforward in real patients. Blood, cerebrospinal fluid and surrounding soft tissue may limit visibility and make an actual implantation much more challenging. Nevertheless, cadaveric studies can be useful as an initial test of feasibility.

Retrospective chart reviews are more prone to compromised internal validity, especially due to selection, and more important, confounding bias<sup>181,182</sup>. A difference between treatment groups may be caused by an inequality of the groups at baseline, and prognostic factors may influence treatment decisions (e.g. antibiotic prophylaxis may be given for a longer period of time in patients with middle ear inflammation during implantation). Although there are statistical methods to control for these types of bias, a randomized trial is the only way to truly avoid these problems. However, because serious complications are rare in cochlear implantation, a large sample size and long follow-up period are needed.



A retrospective chart review can therefore provide valuable information to direct subsequent prospective studies.

## 8.2. Postoperative imaging of cochlear implantation

Computed tomography (CT) is an important tool for evaluating the effects of different surgical approaches and electrode designs on the intracochlear position of the electrode array, and to correlate these results with speech perception scores<sup>155,183-187</sup>. Cone-beam CT (CBCT) has lately been described as a low-dose alternative to multi-slice CT (MSCT) for postoperative evaluation of cochlear implants that has superior image quality<sup>52,188-191</sup>. However, a dose-matched comparison of image quality had never been done.

This study confirms that CBCT requires only a fraction (6 to 16%) of the radiation dose used in clinical MSCT protocols. Some aspects of image quality (e.g. visibility of cochlear inner and outer walls and overall image quality) were positively correlated with radiation dose and therefore rated higher for clinical MSCT than for CBCT protocols. However, when applying dose reduction on MSCT to a dose level similar to CBCT, image quality is comparable to CBCT. Significant differences between systems were found (e.g. in spatial resolution), but not between CBCT and MSCT in general.

These findings contradict the general understanding that, by definition, CBCT is superior to MSCT for cochlear implant imaging, and especially the misconception that the cone-beam technique reduces metal artifacts<sup>192</sup>. Depending on the required information, clinical MSCT may even be preferred over CBCT and there is no need to use or purchase a CBCT scanner especially for these purposes. However, CBCT has other advantages such as allowing scanning in a sitting or supine position and moreover, these results may not apply to the newest generation CBCT scanners, which have a spatial resolution of up to 75 µm (compared to a resolution of around 250 µm in the newest MSCT scanners).

If postoperative CT imaging is necessary (for clinical issues or research questions) and MSCT is being used, it definitely needs to be considered if it is possible to apply a low-dose protocol (comparable to CBCT), especially since the increasing number of radiological examinations may lead to a higher risk of cancer, cardiovascular disease and cataract<sup>193</sup>.

## 8.3. Complications and failures of cochlear implantation

While the number of medical complications reported in cochlear implantation is relatively high compared to other fields of otologic surgery, the variation in reported complication rates is even more notable (6-63%)<sup>37-39,81,82</sup>. This is largely due to the lack of consensus on how to define and grade adverse events. In order to achieve an objective registration of medical complications and make results more comparable, a strict definition of a medical

complication was coined, based on the one provided by the Dutch Federation of Medical Specialists<sup>100</sup> and the recommendations of Jeppesen et al.<sup>39</sup>. Classifying these complications according to a validated system from general surgery (which is based on the type of therapy needed to treat the complication)<sup>95</sup>, further reduces any subjective interpretation of outcomes. Device failures should be distinguished from medical complications and be reported separately (based on international consensus<sup>92,93</sup>).

A relational database system was created, based on forms with input masks and lookup functions, which allows fast and uniform data entry and reduces the risk of errors. This database, in combination with the definitions and classification system mentioned above, proved to be a very suitable method of registering adverse events. Nevertheless, correct registration of medical complications and device failures does not only depend on clear agreements and a suitable database system, but largely on the discipline of the caregivers involved in cochlear implantation.

This database has been made freely available online, along with a manual that contains the definitions and classification system (<http://bit.ly/cidatabasenijmegen>). It is now in use in several international clinics.

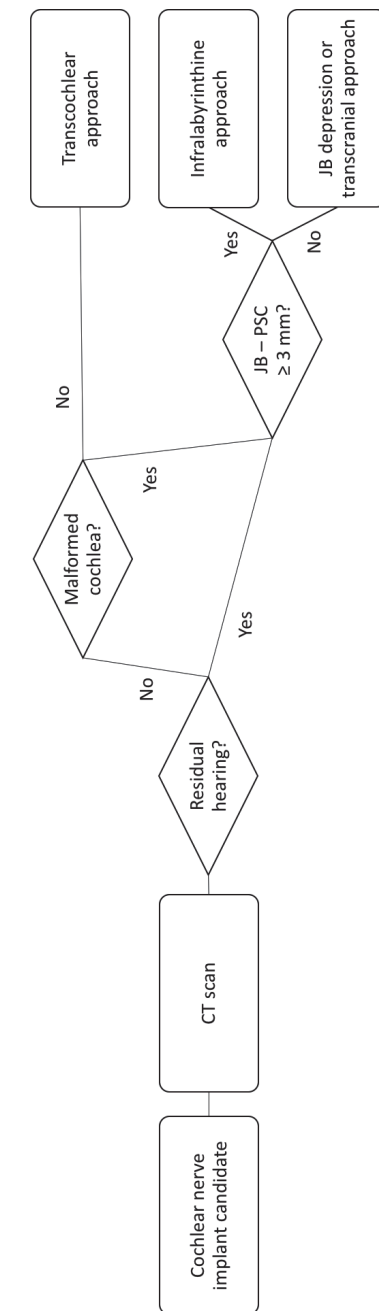
Using this system, analysis of 1362 cochlear implantations that were performed in Nijmegen between 1987 and 2015, revealed a complication rate of 18.4% and a device failure rate of 2.9%. These rates are comparable to those reported in literature. Although most of the complications were minor (87% Clavien-Dindo grade I-II), there were 4 cases of wound infection leading to explantation and 3 cases of postoperative meningitis. In order to be able to prevent such complications in the future, a risk factor analysis was done. This revealed a higher rate of meningitis in patients with an inner ear malformation. Although there are several case reports on the association between inner ear malformation and meningitis<sup>103</sup>, this is the first study to demonstrate the association in cochlear implant patients (without a concurrent CSF leak<sup>97</sup>). No correlation between wound infections and the much-debated regimen of antibiotic prophylaxis<sup>105,194</sup> was found, but there was a higher rate of wound infections in patients who were not vaccinated against *Streptococcus pneumoniae*. The clinical relevance of this finding is unclear since a study on bacterial flora on explanted CIs did not show the presence of *Streptococcus pneumoniae*<sup>106</sup>. Yet both are arguments for pneumococcal vaccine being administered to all patients scheduled for cochlear implantation.

Despite intravenous antibiotics and surgical intervention, serious wound infections often lead to explantation of a cochlear implant, especially in cases with device exposure<sup>98,195</sup>. In 4 patients with a serious wound infection, gentamicin-impregnated collagen sponges have been used in salvage surgery to achieve higher implant survival rates, which was successful in 2 cases. Salvage surgery with gentamicin sponges might save the patient an extra procedure and may lead to significant cost savings, even if only half of the implants are preserved.

## 8.4. Surgical planning and evaluation of cochlear nerve implantation

The limitations of current cochlear implants may be overcome by cochlear nerve implants. Animal studies have demonstrated that indeed, stimulation with a penetrating microelectrode interface leads to a lower spread of excitation, access to low-frequency fibers and lower energy requirements<sup>40</sup>. The next step is to find the most suitable surgical approach for cochlear nerve implantation in humans. Before the development of modern-day cochlear implants, several attempts have been made at cochlear nerve implantation, using a transmastoid-transcochlear approach (in 1957 and 1964<sup>15,18</sup>, see chapter 1.5). This approach has the advantage of being extracranial and similar to that of cochlear implantation. Furthermore, it gives access to the distal end of the cochlear nerve, where it is separated from the facial and vestibular nerves and its movement is limited by its fixation to the cochlea. The optimal vector for such an approach that was determined in 10 3D models based on micro-CT scans of human temporal bones, runs through the anterior edge of the round window and through the inferior portion of the facial recess, intersecting the chorda tympani nerve in 7 out of 10 models. When this vector was used as a reference for the implantation of dummy probes in 3 of the temporal bones, the feasibility of this approach was confirmed, along with the necessity of sacrificing the chorda tympani nerve in 2 out of 3 cases (if cochlear integrity is to be preserved as much as possible). This approach is therefore suitable if cochlear nerve implantation is to be attempted in humans and the vector found in this study may serve as a guideline for drilling the transcochlear opening to the nerve. The dummy probes used for implantation, combined with the morphometric results of the 3D models and postoperative micro-CT scans, could form the basis for the development of a practical clinical device.

Because the first real-life attempts at cochlear nerve implantation will probably be aimed at patients in whom cochlear implantation is difficult (e.g. with obliterated or malformed cochleae) and because eventually, hearing preservation surgery will be preferred, an extracochlear surgical approach also needs to be considered. Transcranial approaches (such as the middle fossa, posterior fossa or retrosigmoid approach) carry the risks of a craniotomy, temporal lobe or cerebellar retraction and often only allow access to the medial part of the internal auditory canal, where nerve separation is poor at best<sup>196</sup>. Therefore, an extended infralabyrinthine approach was used to gain access to the cochlear nerve in 10 human formalin-fixed temporal bones. In 8 out of 10 temporal bones, it was possible to implant a dummy probe into the cochlear nerve. In the remaining 2, a high jugular bulb blocked access to the nerve. Success of the approach was related to the distance between the jugular bulb and the posterior semicircular canal, measured on pre-operative micro-CT scans. Although the extended infralabyrinthine approach is more challenging than the transcochlear approach (1 probe traversed into the facial nerve and in 2 cases, the basal turn was damaged), it is an alternative transmastoid approach that



**Figure 1** Flow chart for choosing the optimal approach for cochlear nerve implantation.

JB: jugular bulb; PSC: posterior semicircular canal.

gives a complete view on the cochlear nerve (allowing a more controlled implantation), and can preserve cochlear integrity. Although further research is necessary to determine the effect of sacrificing the inferior cochlear vein on residual hearing, the chance of hearing preservation is probably higher than with the transcochlear approach. Therefore, the decision to choose for the transcochlear or the infralabyrinthine approach to the cochlear nerve could be based on residual hearing and the presence of a cochlear malformation (especially an absent modiolus). If the distance between the jugular bulb and posterior semicircular canal is smaller than 3 mm, an extended infralabyrinthine approach with depression of the jugular bulb, or a transcranial approach may be considered (Fig. 1).

## 8.5. Directions of future research

This thesis offers several leads for further research. First, a comparison between image quality of the newest CBCT and MSCT scanners could be made in cochlear implant patients to investigate whether results are the same as in this temporal bone study. If that is indeed the case, regular MSCT scanners may be used (applying a low-dose protocol) in research on the effects of new surgical approaches and electrode designs on electrode position, especially in centers where no CBCT scanner is available.

Second, this study has contributed to the identification, classification and quantification of complications as a basis for prioritizing new research. Further studies will be focused on the prevention and treatment of severe wound infections (which may lead to explantation) by investigating biofilm formation and the coating of implants, and prevention and treatment of chronic pain after implantation. Another subject of interest is the prevention of meningitis after cochlear implantation in patients with inner ear malformation. The observation that malformed cochleae give a higher change for meningitis in CI patients will enforce the current thought that patients require recurrent vaccination. Research may be aimed at the identification of (subclinical) perilymphatic fistula in these patients, which can be repaired during implantation, preventing recurrent meningitis<sup>197</sup>.

Third, the field of intraneural implantation offers a broad range of topics for future research. With regard to the surgical approaches, an animal model with human-like anatomy may be used to study the effects of the transcochlear and infralabyrinthine approach on vestibular and cochlear function. In addition, an actual cochlear nerve implant needs to be developed, which may be broadly similar to a contemporary cochlear implant with a multi-shank thin film microelectrode array, as used in this study. New speech processing and mapping strategies will need to be developed, which will probably be more challenging than with conventional cochlear implants. And before proceeding to human implantation, effects of chronic implantation and stimulation may again be studied in an animal model.

V | Closing

9. Summary



The implantable electronic device that in 1957 first provided a sense of sound in a deaf patient, was in fact a cochlear nerve implant. After a few practice sessions, the patient was able to recognize simple words in a closed set. This achievement served as an inspiration for the first cochlear implantation that was conducted in 1961 by William House. From there on, various clinics worldwide contributed to the development of the contemporary multichannel cochlear implant, that has become standard care for restoring hearing in patients with congenital or acquired severe to profound bilateral hearing loss. The history of cochlear implants is further described in chapter 1.

Although the outcome of cochlear implantation has risen far above the initial expectation that it would only be an aid for lipreading, there are still problems to overcome: individual performance variability is high, and speech perception in noise and music perception are limited in most cases. Furthermore, the rate of medical complications reported in cochlear implantation is considerable. This thesis explores three issues that can (directly or indirectly) help solve these problems.

First, new electrode arrays are constantly being developed that intend to improve speech perception in noise and music appreciation by a more selective stimulation of neural populations, stimulating low-frequency nerve fibers and reducing insertional trauma. To evaluate the effects of these new designs, it is vital to assess the intracochlear position of the electrode array in clinical trials, using (preferably low-dose) high resolution imaging techniques. Finding the most suitable low-dose imaging technique is discussed in chapter 2.

Five human cochleae were implanted with a cochlear implant and scanned on two cone-beam computed tomography (CBCT) and two multi-slice compute tomography (MSCT) systems. Four independent observers rated aspects of image quality on a five-point scale, comparing CBCT scans to clinical and dose-matched MSCT scans and declining-dose MSCT protocols to the clinical protocol. CT phantoms were used to determine effective dose and resolution for each acquisition protocol. This confirmed that CBCT requires only a fraction (6 to 16%) of the radiation dose used in clinical MSCT protocols. Some aspects of image quality (e.g. visibility of cochlear inner and outer walls and overall image quality) were positively correlated with radiation dose and therefore rated higher for clinical MSCT than for CBCT protocols. However, when applying dose reduction on MSCT to a dose level similar to CBCT, image quality is comparable to CBCT. Significant differences between systems were found (e.g. in spatial resolution), but not between CBCT and MSCT in general.

Second, in order to reduce the number of medical complications in cochlear implantation, it is necessary to identify the most common and most severe complications. If risk factors can be found for these complications, adjustments in the surgical procedure or perioperative care may lead to a lower complication rate. This topic is elaborated in part III. In chapter 3, a method for the internationally uniform registration and classification of

complications is proposed. A custom database system was developed and made freely available online. Preliminary results showed that it enabled fast and accurate data entry and a medical complication rate of 19.0% in the patients registered thus far. The final results are described in chapter 4: when all 1362 implantations between 1987 and 2015 were registered, the complication rate became 18.4% and a device failure rate of 2.9% was found. Analysis of possible risk factors revealed that there was a higher rate of hematoma in patients with a clotting disorder (5.1 vs. 0.9%,  $p = 0.009$ ) and when a subtotal petrosectomy was performed (13.3 vs. 1.0%,  $p = 0.011$ ), a higher rate of wound infections in patients who were not vaccinated against *Streptococcus pneumoniae* (5.7 vs. 2.6%,  $p = 0.031$ ) and a higher rate of meningitis in patients with an inner ear malformation (2.3 vs. 0.1%,  $p = 0.012$ ). In chapter 5, a novel way to manage serious postoperative infections using implantable gentamicin-impregnated collagen sponges, is reported. This was successful in 2 out of 4 cases.

Third, several limitations of contemporary cochlear implants (such as reduced speech perception in noise and poor music perception) may be overcome by cochlear nerve implants, because placing electrodes in direct contact with the target neurons reduces stimulation thresholds and spread of excitation. Also, low-frequency nerve fibers are more accessible with a penetrating microelectrode array. Because it is therefore worth reconsidering cochlear nerve implantation, the feasibility of penetrating cochlear nerve implantation in humans is explored in part IV. In chapter 6, ten 3D models based on micro-CT scans of human temporal bones were used to simulate a transmastoid-posterior tympanotomy approach to the cochlear nerve that would preserve the osseous spiral lamina, basilar membrane and floor of the scala tympani as much as possible. The optimal vector for such an approach runs through the anterior edge of the round window and through the inferior portion of the facial recess, intersecting the chorda tympani nerve in 7 out of 10 models. When this vector was used as a reference for the surgical approach in 3 of the temporal bones, its feasibility was confirmed, along with the necessity of sacrificing the chorda tympani nerve in 2 out of 3 cases. Postoperative micro-CT scans revealed that the probes were successfully implanted in the cochlear nerve, and the osseous spiral lamina and basilar membrane were intact in all 3 cochleae; however, the probe fully traversed the nerve in only one temporal bone.

In chapter 7, micro-CT scans were obtained of 10 human temporal bones for morphometric evaluation. An extended infralabyrinthine approach was used to gain access to the cochlear nerve and implant a dummy probe, which was possible in 8 out of 10 cases. In the remaining 2, a high jugular bulb blocked access to the nerve, which was related to the distance between the jugular bulb and the posterior semicircular canal in the preoperative scans. Post-operative micro-CT scans confirmed that all probes were implanted in the cochlear nerve, although 1 probe traversed into the facial nerve and in 2 cases, the basal turn was damaged.

In chapter 8, the outcomes of these studies are discussed. It was found that CBCT is adequate for postoperative imaging of cochlear implants. Nevertheless, dose reduction on MSCT can be achieved to a dose level similar to CBCT with an image quality comparable to CBCT. These findings contradict the general understanding that, by definition, CBCT is superior to MSCT for cochlear implant imaging, but these results may not apply to the newest generation CBCT scanners with higher resolution detectors.

The use of a custom database in combination with a strict definition of complications and failures, and a validated classification system proved to be a very suitable method of registering adverse events in cochlear implant surgery. Complication and failure rates are comparable to those reported in literature. The findings of a higher rate of meningitis in patients with an inner ear malformation and an increased rate of wound infections in patients who were not vaccinated against *Streptococcus pneumoniae*, both stress the importance of this vaccination. Salvage surgery with gentamicin sponges seems promising to achieve higher implant survival rates, but further research is necessary to prove this.

Both the transcochlear and extended infralabyrinthine approach are suitable for cochlear nerve implantation. Because the transcochlear approach probably has a higher chance of loss of residual hearing (although further research is necessary to determine the effect of sacrificing the cochlear aqueduct and the inferior cochlear vein in the infralabyrinthine approach), the choice for either approach could be based on residual hearing, distance between the jugular bulb and the posterior semicircular canal and the presence of a cochlear malformation.

Future research could consist of clinical trials that compare the newest MSCT and CBCT scanners for postoperative imaging of cochlear implants, or preventing and treating severe wound infections and meningitis (especially in case of inner ear malformation) after cochlear implantation. Research in the field of intraneural implantation could focus on the effects of chronic implantation and stimulation and comparison with cochlear implantation in an animal model, and the development of an actual implant.

V | Closing

10. Nederlandse samenvatting





Het implanteerbare elektronische apparaat dat in 1957 voor het eerst tot geluidspceptie leidde bij een dove patiënt, was in feite een cochleair zenuwimplantaat. Na een paar oefensessies was deze patiënt in staat om eenvoudige woorden uit een vaststaande reeks te herkennen. Deze prestatie diende als inspiratie voor de eerste cochleaire implantatie, die in 1961 werd uitgevoerd door William House. Sindsdien hebben diverse klinieken wereldwijd bijgedragen aan de ontwikkeling van het hedendaagse multikanaals cochleair implantaat, dat de standaardbehandeling is geworden voor het herstellen van gehoor bij patiënten met een aangeboren of verworven ernstig tot zeer ernstig bilateraal gehoorverlies. De geschiedenis van het cochleair implantaat wordt verder beschreven in hoofdstuk 1.

Hoewel de resultaten van cochleaire implantatie ver uitstijgen boven de aanvankelijke verwachting dat ze slechts een hulpmiddel voor liplezen zouden worden, zijn er nog steeds problemen te overwinnen: er is een grote variatie in individuele uitkomsten, en het spraakverstaan in rumoer en de muziekbeleving zijn in de meeste gevallen beperkt. Verder is het aantal medische complicaties bij cochleaire implantatie aanzienlijk. Dit proefschrift richt zich op drie vraagstukken die (direct of indirect) kunnen bijdragen aan het oplossen van deze problemen.

Ten eerste worden er voortdurend nieuwe elektrodes ontwikkeld met als doel om het spraakverstaan in rumoer en de muziekbeleving te verbeteren door een selectievere stimulatie van neurale populaties, het stimuleren van laagfrequente zenuwvezels en het verminderen van insertie trauma. Om de effecten van deze nieuwe ontwerpen te evalueren, is het essentieel om de intracochleaire positie van de elektrodes te bepalen in klinische trials, door gebruik te maken van (bij voorkeur lage dosis) hoge resolutie beeldvormingstechnieken. Het vinden van de meest geschikte lage dosis beeldvormingstechniek wordt besproken in hoofdstuk 2.

Vijf menselijke cochlea's werden geïmplanteerd met een cochleair implantaat en gescand met twee *cone-beam computed tomography* (CBCT) en twee *multi-slice computed tomography* (MSCT) systemen. Vier onafhankelijke waarnemers beoordeelden aspecten van de beeldkwaliteit op een vijf-punts schaal, waarbij CBCT-scans werden vergeleken met klinische en dosis-gematchte MSCT-scans, en in dosis afnemende MSCT-protocollen met het klinische protocol. CT-fantomen werden gebruikt om de effectieve dosis en resolutie per acquisitieprotocol te bepalen. Dit bevestigde dat CBCT slechts een fractie (6-16%) van de stralingsdosis gebruikt vergeleken met klinische MSCT-protocollen. Enkele aspecten van de beeldkwaliteit (bijvoorbeeld de zichtbaarheid van de cochleaire binnen- en buitenwanden en de algehele beeldkwaliteit) waren positief gecorreleerd met de stralingsdosis en werden daarom hoger gewaardeerd bij klinische MSCT dan bij CBCT-protocollen. Echter, wanneer de dosis van de MSCT-protocollen verlaagd werd tot het niveau van een CBCT-protocol, was de beeldkwaliteit vergelijkbaar met CBCT. Er werden significante verschillen tussen systemen gevonden (bijvoorbeeld in spatiale resolutie), maar niet tussen CBCT en MSCT in het algemeen.

Ten tweede, om het aantal medische complicaties bij cochleaire implantatie te verminderen, is het noodzakelijk om de meest voorkomende en meest ernstige complicaties te identificeren. Als risicofactoren voor deze complicaties kunnen worden gevonden, zou aanpassing van de chirurgische procedure of de peri-operatieve zorg kunnen leiden tot een lager percentage complicaties. Dit onderwerp is uitgewerkt in deel III.

In hoofdstuk 3 wordt een methode voor internationaal uniforme registratie en classificatie van complicaties voorgesteld. Er werd een databasesysteem ontwikkeld en online vrij beschikbaar gesteld. Voorlopige resultaten toonden aan dat hiermee snelle en accurate data invoer mogelijk was en er werd een medisch complicatiepercentage van 19,0% in de tot dan toe ingevoerde patiënten gevonden. De eindresultaten worden beschreven hoofdstuk 4: nadat alle 1362 implantaties tussen 1987 en 2015 waren geregistreerd, werd een complicatiepercentage van 18,4% en een implantaatuitval van 2,9% gevonden. Bij analyse van mogelijke risicofactoren bleek er sprake te zijn van een hoger percentage hematomen bij patiënten met een stollingsstoornis (5,1 versus 0,9%,  $p = 0,009$ ) en wanneer er een subtotale petrosectomie was uitgevoerd (13,3 versus 1,0%,  $p = 0,011$ ), een hoger percentage wondinfecties bij patiënten die niet tegen *Streptococcus pneumoniae* waren gevaccineerd (5,7 versus 2,6%,  $p = 0,031$ ) en een hoger percentage meningitiden bij patiënten met een binnenoor malformatie (2,3 versus 0,1%,  $p = 0,012$ ). In hoofdstuk 5 wordt een nieuwe manier om ernstige postoperatieve infecties te behandelen met implanteerbare, met gentamicine geïmpregneerde collageen sponzen besproken. Dit was succesvol in 2 van de 4 gevallen.

Ten derde, zouden een aantal beperkingen (zoals verminderd spraakverstaan in rumoer en slechte muziekbeleving) van moderne cochleaire implantaten kunnen worden ondervangen door middel van cochleaire zenuwimplantaten, omdat het in direct contact plaatsen van elektrodes met de doelneuronen stimulatierepels en verspreiding van excitatie vermindert. Ook zijn laagfrequente zenuwvezels beter te stimuleren met een penetrerende micro-elektrode. Omdat het hierdoor de moeite waard is om cochleaire zenuwimplantatie te heroverwegen, wordt de haalbaarheid van penetrerende cochleaire zenuwimplantatie bij mensen onderzocht in deel IV. In hoofdstuk 6, werden tien 3D-modellen van micro-CT-scans van menselijk ossa temporalia gebruikt om een transmastoidale-posterieure tympanotomie benadering van de cochleaire zenuw te simuleren, waarbij de benige lamina spiralis, de membrana basilaris en de bodem van de scala tympani zoveel mogelijk intact zouden blijven. De optimale vector voor een dergelijke benadering loopt door de voorste rand van het ronde venster, door het onderste gedeelte van de recessus facialis en kruist de chorda tympani in 7 van de 10 modellen. Wanneer deze vector werd gebruikt als referentie voor de chirurgische benadering in 3 van de ossa temporalia, werd de haalbaarheid bevestigd, samen met de noodzaak van het opofferen van de chorda tympani in 2 van de 3 gevallen. Uit post-operatieve micro-CT-scans bleek dat de probes met succes geïmplantieerd waren in de

gehoorzenuw en de lamina spiralis en membrana basilaris intact waren in alle 3 de cochleas; echter doorkruiste de probe in slechts één geval de zenuw volledig.

In hoofdstuk 7 werden micro-CT-scans van 10 menselijke ossa temporalia vervaardigd voor morfometrische evaluatie. Een uitgebreide infralabyrintaire benadering werd gebruikt om toegang tot de gehoorzenuw te verkrijgen en een dummy probe te implanteren, hetgeen in 8 van de 10 gevallen mogelijk was. In de resterende 2 blokkeerde een hoge bulbus jugularis de toegang tot de zenuw, en dat bleek gerelateerd te zijn aan de afstand tussen de bulbus jugularis en het posterieure semicirculaire kanaal in de preoperatieve scans. Met postoperatieve micro-CT-scans werd bevestigd dat alle probes in de nervus cochlearis geïmplantieerd waren, hoewel 1 probe in de nervus facialis door liep en in 2 gevallen de basale winding beschadigd werd.

In hoofdstuk 8 worden de uitkomsten van deze onderzoeken besproken. Het bleek dat CBCT adequaat is voor postoperatieve beeldvorming van cochleaire implantaten. Niettemin kan verlaging van de dosis van MSCT worden bereikt tot het niveau van CBCT, met een beeldkwaliteit die vergelijkbaar is met CBCT. Deze bevindingen spreken de algemene veronderstelling tegen dat CBCT per definitie superieur is aan MSCT voor beeldvorming van cochleaire implantaten, maar deze resultaten zijn mogelijk niet van toepassing op de nieuwste generatie CBCT-scanners met hogere resolutie detectoren.

Het gebruik van een *custom-made* database in combinatie met een strikte definitie voor complicaties en implantaatuitval, en een gevalideerd classificatiesysteem bleek een zeer geschikte methode voor het registreren van nadelige uitkomsten bij cochleair implantaatchirurgie. De percentages van complicaties en implantaatuitval zijn vergelijkbaar met die in de literatuur. De bevindingen van een hoger percentage van meningitis bij patiënten met een binnenoor malformatie en een verhoogd aantal wondinfecties bij patiënten die niet tegen *Streptococcus pneumoniae* gevaccineerd waren, benadrukken beiden het belang van deze vaccinatie. Chirurgische behandeling met gentamicine sponzen lijkt veelbelovend om een hogere implantaatoverleving te bereiken bij ernstige wondinfecties, maar verder onderzoek is nodig om dit te bewijzen.

Zowel de transcochleaire als de uitgebreide infralabyrintaire benadering zijn geschikt voor cochleaire zenuwimplantatie. Omdat de transcochleaire benadering waarschijnlijk een hogere kans geeft op verlies van het restgehoor (hoewel verder onderzoek nodig is om het effect van het opofferen van de aqueductus cochlearis en de vena cochlearis inferior in de infralabyrintaire benadering te bepalen), kan de keuze voor een bepaalde benadering gebaseerd worden op de aanwezigheid van restgehoor of een cochleaire malformatie, en de afstand tussen de bulbus jugularis en het posterieure semicirculaire kanaal.

Toekomstig onderzoek zou kunnen bestaan uit het vergelijken van de nieuwste MSCT- en CBCT-scanners voor postoperatieve beeldvorming van cochleaire implantaten, of de preventie en behandeling van ernstige wondinfecties en meningitis (vooral bij binnenoor malformatie) na cochleaire implantatie. Onderzoek op het gebied van intra-

neurale implantatie zou zich kunnen richten op de effecten van chronische implantatie en stimulatie, een vergelijking met cochleaire implantatie in een diermodel, en de ontwikkeling van een klinisch bruikbaar implantaat.

## VI | Appendices

### 11. References



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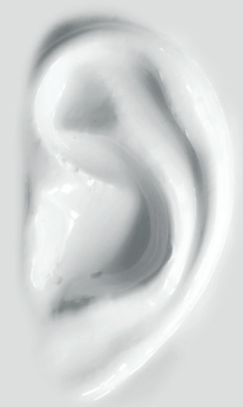
### 12. List of abbreviations



CA:	cochlear aqueduct
CBCT:	cone-beam computed tomography
CI:	cochlear implant
CN:	cochlear nerve
CSF:	cerebrospinal fluid
CTDI:	computed tomographic dose index
CTN:	chorda tympani nerve
CV:	coefficient of variation
DNE:	distal nerve end
EILA:	extended infralabyrinthine approach
FC:	falciform crest
FN:	facial nerve
FWHM:	full-width at half maximum
GPN:	greater petrosal nerve
HU:	Hounsfield units
IAC:	internal auditory canal
ICU:	intensive care unit
ICV:	inferior cochlear vein
IVN:	inferior vestibular nerve
JB:	jugular bulb
ME:	middle ear
MMA:	mid-modiolar axis
MPR:	multi-planar reconstruction
MSCT:	multi-slice computed tomography
MT:	mastoid tip
OSL:	osseous spiral lamina
PAN:	posterior ampullar nerve
PFD:	posterior fossa dura
PSC:	posterior semicircular canal
PSF:	point-spread function
RW:	round window
TB:	temporal bone
SF:	singular foramen
SS:	sigmoid sinus
ST:	scala tympani
SV:	scala vestibuli
SVN:	superior vestibular nerve

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### 14. Curriculum Vitae





Erik Theunisse werd op 7 december 1982 geboren in Nijmegen. Hij groeide op in Beuningen en behaalde zijn gymnasiumdiploma aan het Canisius College in Nijmegen. Hij studeerde Geneeskunde aan de Radboud Universiteit. Tijdens zijn studie volgde hij het interdisciplinaire Honours Programma en was onder andere actief als praeses van de medische faculteitsvereniging (MFVN). Na zijn studie startte hij als arts-onderzoeker aan de afdeling KNO-heelkunde van het Radboud umc, waar hij in 2010 begon aan zijn opleiding tot KNO-arts. Gedurende zijn opleiding was hij enkele jaren voorzitter van de arts-assistentenvereniging (AAVR) en nam hij zitting in de Centrale Opleidings Commissie. Hij differentieerde zich in de Otologie en is sinds 2016 werkzaam in het Canisius-Wilhemina ziekenhuis als KNO-arts met als aandachtsgebied de sanerende en reconstructieve oorchirurgie. Hij woont sinds 2010 samen met Leonie en is de trotse vader van Willem en Guus.

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### 15. List of publications



*Theunisse HJ*, van den Hoogen FJ. Airway obstruction due to inflammatory myofibroblastic tumour of the posterior pharyngeal wall. *J Laryngol Otol*. 2011 Jun;125(6):655-9.

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